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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 36.] 1939. [No. 11.

SUMMARY OF RECENT ABSTRACTS.

IX. LEPROSY.*

Classification.—RABELLO (p. 290) suggests a method, for the details of which the original abstract should be consulted, and WADE (p. 290) has also contributed to this subject. RYRIE (p. 550) uses a method in which letters are employed to signify the resistance of the patient, and KUSNETZOW (p. 550) advises that four phases of the disease should be recognized.

Epidemiology.—There are a few lepers still in Great Britain, but MACLEOD (p. 545) shows that the majority are adults who have returned from tropical countries. In Italy the same process is occurring in peasants who return after emigrating to Latin America. BROCCHIERI (p. 285) quotes the case of a woman who had never been away from Italy and gave no history of contact, but who acquired leprosy probably, he considers, through contact with a returned leprous emigrant.

In Estonia, PARMAKSON (p. 883) shows that cutaneous disease is more common than neural. Women are more frequently attacked than men and the highest incidence is in the age groups 30–39. The average duration to death was 15 years and 19·3 per cent. of patients recovered under treatment, of whom 11·4 per cent. later relapsed.

DALGAMOUNI (p. 558) estimates that there are 15,000 lepers in Egypt. He describes the work done in the clinics.

In S.E. Nigeria, OBERDÖRFFER (p. 882) found from 3 to 5 per cent. of the population to be infected, but there were comparatively few women and children affected (but see below, DAVEY). The disease was most active in the dry months, and he associates high rates with the consumption of coco-yams, which contain toxic substances. DAVEY (p. 882) reports that it is the native custom to segregate lepers in small villages close to the main villages, but in one main village there still remained 65 lepers. In the areas examined, female cases outnumbered male by almost 2 to 1. Slightly higher female than

* The information from which this series of summaries has been compiled is given in the abstracts made by the Sectional Editors in the *Tropical Diseases Bulletin*, 1938, Vol. 35. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

male rates were found in the lower Congo by the FORÉAMI staff (p. 284) and the total rate varied from 1·7 to 4·3 per 1,000. In Basutoland, GERMOND (p. 286) reports a rate of 3·2 per 1,000, of which 90·5 per cent. were mild neural cases. STRACHAN (p. 285) shows, in the same country, that the average age on admission to hospital was 36·5 years and all except a quarter had had the disease for less than 2 years on admission.

CILENTO (p. 287) reports that leprosy is a serious problem in New Guinea and that increasing numbers are being found in the Solomon Islands. AUSTIN (p. 546) from Makogai shows that it is more severe in Fijians than in Indians.

Contact.—The subject of contact is touched upon by several authors. MOISER (p. 881) considers that leprosy is spread in S. Rhodesia during native beer drinks and advises that lepers should, therefore, be prohibited from taking part. In French Equatorial Africa LE BIHAN (p. 545) found a very high proportion (1,182 of 1,832 cases) of direct family antecedents. He considers that goitre, which is very prevalent, does not predispose to the disease, but that elephantiasis does. In Bengal LOWE (p. 883) found contact history in 80 per cent. of cases. The incidence was 4·38 per cent., and infections were found mainly in early life and mainly in males, in whom the disease was severe. The majority of patients showed neural infections. Infection was traced to open cases in half of the patients reported by COCHRANE and RAJAGOPALAN (p. 885), who found a rate of 6 per cent. in a school survey in Madras.

INNES (p. 882) considers the distribution in the British Solomon Islands to be that of a small group or family disease, and found an incidence rate of 1·02 per cent. [see CILENTO above]. At the Nauru Island segregation camp CLOUSTON (p. 291) shows that 5 of 24 children, born to lepers but separated at once from their parents, developed the disease after the age of three. It was not, however, possible to be certain that no contact had taken place with other lepers on the island.

On the other hand, in the Dutch East Indies LAMPE (p. 884) found that infections other than familial account for 66 to 80 per cent. of cases and only rarely were as many as three cases found in one family.

MCCOY (p. 557) stresses the importance of family transmission, but admits that the exact mode is uncertain. He does not (p. 545) think that climatic conditions can explain the varying trends of leprosy in the United States, nor does he see convincing evidence that any control measure yet attempted has been successful in retarding spread, though he approves of attempts by the colony method. AYCOCK and MCKINLEY (p. 884) think that inherited susceptibility is a factor in contact spread.

In an examination of 15,424 contacts in Mexico URUEÑA (p. 546) reports that 98 patients, who would ordinarily have escaped observation, were found. Housing conditions were bad and 6,739 persons, including 2,717 children, were living in the same rooms as lepers. Serious nodular cases accounted for 30·1 per cent. of the 3,882 lepers studied. In the Argentine BALIÑA and BASOMBRÍO (p. 881) show that the incidence on the coast is higher than in the dry Andes area, which supports the theory of ROGERS of the influence of humidity. High density of population also favours high incidence, but conjugal infection was rare in the series examined, and only occurred in bacillary positive cutaneous cases. In three-quarters of 862 cases the first symptoms were cutaneous. DO PATEO and PEREIRA (p. 286) advise

weekly examinations of contacts so that treatment can be commenced at an early stage. The majority of contacts who develop disease do so within 3 years, but the interval may be 5 years or more. PORTUGAL (p. 284) records the following contact figures: family 11 per cent., conjugal 9·2 per cent., other 16·7 per cent. The heaviest incidence in the 873 cases studied occurred between the ages of 20 and 40, and in general males were rather more frequently attacked than females. Cutaneous and mixed forms accounted for from half to two-thirds in different areas.

Bacteriology.—ADLER (p. 293) succeeded in infecting the Syrian hamster, *Cricetus auratus*, with material from human leprous nodules, having previously removed the spleens of the animals. Evidence of multiplication of bacilli was obtained in 3 of the 4 animals used, and of generalization in one of the three. With ASHBEL (p. 888) he showed that leprosy bacilli in thin sections of tissue dried over sulphuric acid were still able to infect hamsters after 7 days. WATANABE (p. 888) has succeeded in subtransplanting for three generations granulating tissues resulting from inoculation of human leprosy material into rats previously treated with venom.

Cultivation.—MCKINLEY and DE LEON (p. 292) have subcultured the bacilli isolated in 1931 through 60 generations, during which no luxuriant growths have developed. This is in contrast with the experience with other acid-fast bacilli thought to be *Myco. leprae.* They describe a gas tension incubator for mass culture in controlled atmospheres, used in conjunction with hormone glycerol agar medium. SALLE and MOSER (p. 292) used this gas environment, which is based on an oxygen-carbon dioxide mixture, and succeeded in cultivating *Myco. leprae* on glycerine veal agar slopes. They were also successful in cultivation on glycerine veal agar with the addition of embryonic chick tissue. Positive results, with acid-fast and non-acid-fast rods, were obtained in 190 of 311 tubes and flasks when the inoculum consisted of nodules removed aseptically and minced.

FAURE-BEAULIEU and BRUN (p. 887) claim to have cultivated the organism and to have found mutation between the acid-fast and non-acid-fast granules which they have observed in leprosy lesions. PAPAIOANNOU (p. 892) reports successful cultivation and transmission of human and rat leprosy bacilli to various rodents.

MANALANG (p. 887) also reports acid-fast and non-acid-fast forms of *Myco. leprae* in both treated and untreated lesions, the latter being regarded as young or degenerating forms. In glands kept *in vitro* with preparations of *H. wightiana*, especially when these are applied intermittently, the acid-fast forms largely change to the non-acid-fast. This may explain the greater efficiency of intradermal injections of these preparations when they are applied intermittently.

ANDERSON *et al.* (p. 294) report on the chemical constitution of acetone-soluble fat of *Myco. leprae.*

Since ordinary methods of disinfection fail to remove leprosy bacilli, living or dead, from instruments, BEAUDIMENT and TIVOLLIER (p. 888) recommend 1 to 2 per cent. of soda for this purpose.

RADNA (p. 551) reports positive bacteriological results in the examination of the sediment of dehaemoglobinized venous blood in 84·31 per cent. of cutaneous and mixed cases. LLERAS ACOSTA (p. 551) has isolated an acid-fast bacillus in culture experiments on the blood of patients with nodular disease. He used Petragnani's medium and succeeded in 20 of 66 patients. With this bacillus as antigen,

he found positive complement fixation tests to be given by 99·38 per cent. of bacteriologically confirmed lepers, 92·5 per cent. of clinically diagnosed lepers, 11·38 per cent. of children of lepers, 18·48 per cent. of healthy contacts and 38·12 per cent. of cured patients. Only 0·09 per cent. of normal persons were positive. Intradermal tests performed with a " leprolin " prepared from the bacillus were positive in normal controls and negative in lepers, which he explains as an indication of immunity. [See also SATÔ below.] SAENZ (p. 887) repeated these serological tests, but used as antigen an acid-fast bacillus obtained from tap water; his results were identical with those obtained by LLERAS ACOSTA. He found also that the two bacilli produced, on intradermal injection, the same reactions as were given by other acid-fast saprophytes. SATÔ (p. 559) recovered 14 strains of saprophytic acid-fast bacilli from 30 rats infected with rat leprosy. Serological tests with a variety of antigens, including preparations of leprosy and tubercle tissues, produced positive results in from 0 to 25 per cent. of infected rats and in from 5 to 100 per cent. of human leprosy infections. Normal rats and healthy persons were all negative. By precipitin tests, HENDERSON (p. 292) found group affinity in 13 of 15 strains of acid-fast bacilli isolated from lepers, and shows that these strains have a group relationship with *Myco. phlei.* [The findings of the three latter workers do not invalidate the claim that the bacillus of Lleras Acosta is useful in the serological diagnosis of leprosy, but they constitute a strong argument against its specificity. The finding of acid-fast bacilli in blood, which in such work is usually treated with various reagents, has in recent years been a highly controversial subject.]

RABELLO and PINTO (p. 889) found the Witebsky, Klingenstein and Kuhn complement fixation test (with a tuberculin antigen) to be positive in 68 per cent. of tropho-neurotic cases, 60 per cent. of macular cases and negative in 70 per cent. of cutaneous. This is the opposite of the results of the Mitsuda test.

Positive Wassermann and Kahn tests in mild and early cases are considered by MUIR and ROY (p. 552) to indicate coincident spirochaetal disease, but not necessarily so in advanced cases, especially if subject to leprosy fever. GUNDERSEN and BERNER (p. 552) regard them as indicating syphilis.

Skin tests.—In the *Monthly Bulletin of the Bureau of Health,* Manila (p. 295) is a statement of the results of 5,174 skin tests performed with products derived from different types of acid-fast organisms including those isolated from cases of leprosy and the strains cultivated by McKINLEY and SOULE [see McKINLEY and DE LEON above]. In no instance did the positive reactions in leprosy exceed the negative, and no definite conclusions can therefore be drawn.

The leprolin test was used by CAMPOS (p. 553) on 331 healthy children of lepers. He found that positive results increased with age, from 22·6 per cent. under 3 years to 86 per cent. over 13. Children removed from parents at birth were negative. The test is negative in the uninfected and the heavily diseased, and positive in healthy contacts and in those with slight lesions. RADNA (p. 889) similarly reports negative reactions to the Mitsuda test in active cutaneous, and positive in nerve and recovering cases. A positive result in a previously negative case is a good sign. RODRIGUEZ (p. 553) regards negative results in cutaneous cases as due to anergy and positive

reactions in such cases as constituting a favourable sign. PARMAKSON's results (p. 554) support this latter conclusion.

Clinical.—Sternal puncture was used in diagnosis by LOWE and DHARMENDRA (p. 291) who found acid-fast bacilli in 16 of 32 patients with nodular disease, but in only 1 of 18 nerve cases. Gland puncture yields the bacilli in nodular disease but VAN BREUSEGHEM (p. 291) finds it of no value in nerve leprosy. He uses a sweating test by covering the area of skin with Tr. iodi, allowing to dry, covering with starch and then attempting to provoke sweating by light exercise. If sweating occurs the starch is turned blue.

DUBOIS *et al.* (p. 290) point out that histological diagnosis in early leprosy is not always certain, and confusion with tertiary yaws may occur.

Tuberculoid leprosy.—RABELLO (p. 548) argues that tuberculoid leprosy presents clinical and pathological changes similar to those seen in the Besnier-Boeck sarcoid and Schaumann's syndrome, but REENSTIERNA, admitting the similarity of the skin lesions and of the radiological appearances in bones and lungs, states that the leprosy bacillus has not been shown to be capable of producing the systemic reactions of Schaumann's syndrome. FERNÁNDEZ (p. 289) regards the tuberculoid leprous reaction as an allergic phenomenon with intense tissue reaction in the early stages and later necrosis, due to invasion of the sensitized tissues by the bacilli, which increase in number as the reaction diminishes. DA ROSA (p. 550) holds that the lepra reaction is allergic but that it is not specific since the bacilli are not found in the skin.

HUGHES (p. 547) regards the tuberculoid form as a stage in the natural evolution of immunity, so that it is common in races which have for long been associated with leprosy.

TISSEUIL (p. 289) describes 4 cases in which tuberculoid lesions, thought to be primary leprous chancres, were present in children. In 42 neural cases in Madras, 7 were classed as major tuberculoid, 6 as minor tuberculoid or intermediate, 5 as retrogressive papulate and 24 as simple, by WADE *et al.* (p. 547). WADE and FRASER (p. 289) report that tuberculoid lesions are fairly common in S. China, being found clinically in 23 of 225 patients examined. In all except 1 of 31 neural cases from which biopsy material of the leprides was taken tuberculoid changes were seen.

WADE *et al.* (p. 885) describe the microscopical changes in nerve lesions. Activation may be related to climatic conditions. Changes in the finger prints of 12 per cent. of neural cases, 9 per cent. of macular and mixed, and 6 per cent. of nodular cases are reported by VIEIRA and DE ABREU (p. 547). The changes are first evident in the little and ring fingers, which points to ulnar distribution.

MITSUDA and NAGAI (p. 288) attribute the alopecia frequently seen in leprosy, over the course of the larger veins, to infiltration of the perivascular lymph spaces and consequent pressure around the hair papillae, causing malnutrition and atrophy.

OBERDÖRFFER (p. 284) found nasal lesions in 62 per cent. of patients in the Itu leper colony in S. Nigeria. These were mostly localized, especially on the anterior nasal septum.

The basal metabolism in leprosy, according to JUNIOR (p. 288) is increased, but in quiescent cases tends to fall to normal. The leprotic reaction increases the rate.

RYRIE (p. 886) from an experience of 600 cases, shows that leprosy does not influence pregnancy, but pregnancy causes slow progressive spread of the disease in the later months, probably through mineral depletion, since the exhibition of calcium tends to check this aggravation. The placenta and cord are not affected and children removed at birth remain healthy.

NAKAJYO and SUZUKI (p. 294) obtained cultures of tubercle bacilli from the sputum of 30 lepers in 100 examined.

Control and treatment.—In the Sudan it is held that although leprosy is well under control, improved diet and standards of living will be necessary for its permanent eradication (p. 286). CILENTO (p. 287) advises re-examination of contacts for every 6 months for 5 years in Australian territories. For the aboriginals only segregation is likely to be effective, since they fear medical treatment. The development of agricultural and industrial work by inmates of leper colonies is shown by reports from N. Nigeria (p. 284), Basutoland (p. 285) and Egypt (p. 286). But in connexion with segregation MUIR (p. 546) considers that compulsion should only be applied by the community itself—never from without. Treatment by general methods, combined with chaulmoogra, is important.

Chaulmoogra.—A comprehensive account of this and allied oils has been written by SCHLOSSBERGER (p. 296), and LOWE and DE (p. 556) give tests for the suitability of hydnocarpus oil for injection. Decomposition of the esters of *H. wightiana* oil is responsible for irritation occasioned on injection. This can be removed, according to COLE and CARDOSO (p. 296) by neutralization and blowing out with steam. LABERNADIE and GUICHARD (p. 890) report that the neutralization of hydnocarpus oil by the procedure of Le Naour and Roubaud yields a product free from glycerine but in which the content of active glycerides is slightly increased [not, as stated in the original abstract, " containing little active glyceride "]. BARÉ (p. 891) reports success with intravenous neutralized chaulmoogra oil.

WOODMAN (p. 295) speaks favourably of chaulmoogra treatment in early leprosy in the Sudan, and of the value of settlements in segregation, and MOISER (p. 881) reports that 80 per cent. of patients obtained benefit from moogrol treatment in a hospital in S. Rhodesia. At the Uzuakoli Leper Colony in N. Nigeria a mixture of hydnocarpus oil, 25 per cent., its esters, 25 to 62½ per cent., with 12½ per cent. of cod liver oil, 12½ per cent. olive oil and 4 per cent. creosote in doses of 1 to 10 cc. is used for treatment by injection (p. 284).

Intradermal treatment is reported by STRACHAN (p. 286) to be popular in Basutoland. LIMA (p. 554) speaks highly of the intradermal infiltration of chaulmoogra and its derivatives: the majority of patients are improved but chaulmoogra does not seem to have any effect on ocular lesions. VALLE (p. 549) in fact, states that these preparations are liable to provoke dangerous reactions in lesions of the eye and therefore advises that they should not be used in such complications. The anterior segment of the eye may be invaded from the lids, and cauterization, peritomy and iridectomy may be necessary to prevent invasion. He endorses the value of trypan blue treatment.

In tuberculoid lesions RYRIE (p. 555) finds intradermal chaulmoogra esters of little use, though this method is the best in cutaneous disease with abundant bacilli. Subcutaneous hydnocarpus oil gave the best results in a series of tuberculoid cases. He (p. 885) describes the acute sloughing tuberculoid disease which is only seen in Malaya and

which is intractable except by large local injections of hydnocarpus oil and inunctions of hydnocarpus ointment. On the other hand TISSEUIL (p. 556) obtained disappearance of tuberculoid lesions by intradermal injections of chaulmoogra oil. Olive oil was inert.

In ulceration of the foot LOWE and CHATTERJI (p. 297) advocate the injection of hydnocarpus preparations along the course of the tibial nerve, since infiltration of that nerve is present in such cases. Surgical decapsulation of the nerve relieves pain but does not induce healing. BOUSEFIELD (p. 549), after removal of necrosed bone, uses mild antiseptic solutions of 0·5 to 2 per cent. copper sulphate together with intramuscular and local intradermal injections of iodized chaulmoogra esters. This treatment combined with plentiful good food is very successful.

PAGET (p. 297) investigated the components of the oil of *Carpotroche brasiliensis* which is used for treatment of leprosy in Brazil, and which contains the characteristic chaulmoogric and hydnocarpic acids. TISSEUIL *et al.* (p. 890) report that ground nut oil has only a feeble action in leprosy, but that Gorli butter produces slow improvement in tuberculoid cases. TISSEUIL (p. 298) reports favourable results with synthol soufré in the treatment of perforating ulcers.

Methylene blue.—LE BIHAN (p. 545) advocates this drug for pains when combined with chaulmoogra treatment. Remarkable and promising results are reported by DE ALMEIDA and DE MOURA COSTA (p. 889) from the administration of 2 or 3 intravenous injections of 5 to 10 cc. methylene blue [strength not stated] followed, when the drug is no longer being excreted in the urine, by placing the patient in a pressure of 2·5 to 3·5 atmospheres of oxygen for varying periods. Clinical improvement occurs with great alteration and diminution of the bacilli in the lesions. The treatment is based on the fact that anaerobic organisms cease to develop under an oxygen pressure of 4 to 5 mm. mercury. ROGERS suggests a trial of this method with chaulmoogra in place of the methylene blue.

To overcome the reactions which occur to intravenous methylene blue TISSEUIL (p. 891) uses intravenous injections of 0·1 per cent. of that drug in 4 per cent. glucose and 0·4 to 0·9 per cent. saline. If fever persists the injections should be stopped for a time.

Other drugs.—TISSEUIL (p. 300) reports 4 patients with laryngeal leprosy relieved rapidly by yohimbine by the mouth. FLORIANI and FLORIANI (p. 298) used a 2·5 per cent. aqueous solution of the total alkaloids of the bark of *Aspidosterma polyneuron* in the Argentine for intramuscular injection in leprotic ulceration. Good results were obtained in 15 cases. Others were given preparations of *Bixa orellana*, and both drugs are advocated.

Tellurium and its sodium salt retard the development of rat leprosy, diminishing the vitality of, but not killing the bacilli. MARCHOUX and CHORINE (p. 297) used the method in man but the results, though beneficial, were not lasting. Carbon dioxide snow proved useful in a case of leprosy with extensive rose coloured annular plaques treated by VIGNE *et al.* (p. 299).

Vaccines and Sera.—PEREIRA (p. 299) reports apparent benefit from the use of Vaudremer's vaccine in those with fever and debility and in early nerve lesions. In ocular cases it may be dangerous and it has no effect on nodules, ulcers or sensory disturbances. Temporary improvement due to antirabic vaccine is attributed by TISSEUIL and GUILHAUMOU (p. 299) to simple biotherapy. REENSTIERNA (p. 299)

obtained beneficial results in S. America from the use of the serum he has prepared. He does not think that it alone will effect cure, but considers it to be a useful auxiliary treatment.

Others.—RADNA (p. 891) reports uniform relief of leprosy pain following the use of a preparation of cobra venom, and GASS (p. 891) obtained similar results.

Anti-leprotic treatment proved harmful in a leper with syphilitic ulceration of the palate, but NODENOT (p. 557) reports that healing took place under anti-syphilitic treatment alone.

Removal of three leprous nodules, a few weeks after their appearance, from the head of a French priest working in a leper settlement in Hawaii has apparently prevented any spread during four years. Presumably the infection was transmitted to the skin of the head directly from the fingers after handling the patients. WAYSON (p. 300) in reporting this mentions a similar case in a child operated upon by McCOY and remaining healthy for 16 years.

C. Wilcocks.

BLACKWATER FEVER.

PRÉCIS OF ABSTRACTS IN THIS SECTION.

FAIRLEY and BROMFIELD (p. 885) discuss the nature of pseudo-methaemoglobin which they now propose to name methaemalbumin. It is never found in the corpuscles and never appears in the urine. VALCKE and VAN DEN BERGHE (p. 886) describe a case of nocturnal haemoglobinuria in which the attacks were precipitated, especially by anti-anaemia treatment. Pseudo-methaemoglobin [methaemalbumin] was found in the blood.

ISMAIL and SOLIMAN (p. 886) describe two cases of blackwater fever in Egypt, where it is rare, and appear to suggest an allergic process in the causation. MARSCHALL (p. 887) also considers an explanation on allergic lines to be probable. The disease is extremely rare in Porto Rico though fairly common in the other islands of the Great Antilles.

FOY and KONDI (p. 887) find little evidence of heavy malarial infection just prior to the onset of blackwater. They discuss the mechanism for disposal of pigment and find more than a casual relationship between the taking of quinine and the onset of blackwater, though blackwater does occur after atebrin.

SARCINELLA (p. 888) also refers to quinine as a determining factor and suggests that in small doses it may act by virtue of its stimulating action on particularly resistant parasites.

THOMAS and MILLEN (p. 888) record blackwater in a pregnant woman, which is not usual. The attack followed the taking of quinine for an attack of malaria. GUNTHER (p. 889) also describes blackwater in pregnancy. His patient developed it after a dose of atebrin.

LAFFERRE (p. 889) reports a patient who had a relapse of malignant tertian malaria after blackwater fever.

KRISHNAN (p. 889) has treated 7 patients with glucose, ascorbic acid and cortin and records beneficial results with complete recovery in all, but YORKE comments that further evidence is necessary before proof of benefit is established. *C. W.*

FAIRLEY (N. Hamilton). **Methaemalbumin (Pseudo-Methaemoglobin).** [Correspondence.]—*Nature.* 1938. Dec. 31. Vol. 142. No. 3609. pp. 1156–1157.

—— & BROMFIELD (R. J.). **I. Pseudo-Methaemoglobin—its Synthesis from Crystalbumin and Alkaline Haematin. II. Pseudo-Methaemoglobin—its Demonstration in the Marchiafava-Micheli Syndrome of Nocturnal Haemoglobinuria.** [Demonstration.]—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1939. Jan. 28. Vol. 32. No. 4. pp. 431–433.

In a previous paper Fairley suggested the name pseudo-methaemoglobin for a new blood pigment, formerly confused with methaemoglobin, found in the plasma of blackwater fever cases. [This *Bulletin*, 1937, Vol. 34, p. 841.] This pigment is derived from extracorpuscular oxyhaemoglobin. Fairley has since demonstrated the same pigment in nocturnal haemoglobinuria, incompatible transfusion and pancreatic cyst fluid.

It has long been recognized that, on incubation, solutions of haemoglobin yield methaemoglobin and later haematin. Fairley showed that when oxyhaemoglobin was incubated at 40°C. for 24 to 72 hours in the presence of human plasma, pseudo-methaemoglobin was produced. Similarly, when alkaline haematin was added to human plasma or serum, pseudo-methaemoglobin immediately appeared. This suggested that haematin was coupling with some protein to form a new compound. Apparently only human and simian plasma contained the constituent coupling with haematin to form pseudo-methaemoglobin.

Further work showed that alkaline haematin produced pseudo-methaemoglobin only with the albumin fractions and never with the pseudo-globulin or euglobulin fractions of serum protein. Of the albumin fractions, only crystalbumin proved capable of forming pseudo-methaemoglobin. Finally, it was noted that whilst the intravenous injection of alkaline haematin into *Macacus rhesus* produced pseudo-methaemoglobin, similar injections failed to produce it in rabbits.

Certain details are given concerning the spectrum of the synthesized pigment and its chemical and physical behaviour. From this work it is concluded that pseudo-methaemoglobin is modelled on the methaemoglobin pattern ; but that while the prosthetic group is similar, the protein component is native serum albumin instead of native globin. The iron is held in the trivalent state and is even more resistant to reducing agents than methaemoglobin itself. In view of these findings, Fairley proposes to change the name of pseudo-methaemoglobin to methaemalbumin.

It is noted that as methaemalbumin is never found within the corpuscles it cannot function as a respiratory pigment. It is derived from circulating extracorpuscular haemoglobin liberated during intra-vascular haemolysis, or from blood which has escaped into

cysts or other cavities. The molecular size of methaemalbumin renders it impermeable to the kidney, and for this reason it never appears in the urine. *W. Yorke.*

VALCKE (G.) & VAN DEN BERGHE (L.). Le syndrome de Marchiafava-Micheli (hémoglobinurie nocturne). Observation clinique. [**The Marchiafava-Micheli Syndrome.**]—*Ann. Soc. Belge de Méd. Trop.* 1939. June 30. Vol. 19. No. 2. pp. 235–240.

The patient who forms the subject of this note had spent two periods in the Belgian Congo, the first from 1928 to 1931 and the second from 1932 to June, 1935. He had apparently been in perfect health and had not suffered from malaria. During the winter of 1935, when in Belgium, he suffered from a cold and one morning, after a normal night, he noticed that the urine was black. This was not accompanied by pain or any other symptom. The black urine persisted for two days. The patient consulted a doctor, who diagnosed blackwater fever.

At the commencement of his third tour in the Congo in May, 1936, the same symptoms reappeared during a fatiguing journey ; the urine was black in the morning, but less dark during the afternoon and evening ; there were no other symptoms, and again the attack lasted for two days. In November, 1936, there was a similar attack and others followed in November, 1937, and in June, 1938. The doctor who was consulted at the last attack discovered a pronounced anaemia. He ordered a normal diet with iron and atebrin. In August, 1938, a series of ten daily injections of 2 cc. of liver extract was given ; each of these injections was followed the next morning by the passage of black urine. In view of this, the doctor decided to increase the injections to 5 cc. and to administer them only every other day. After the third injection, however, it was necessary to stop treatment in view of the fact that the haemoglobinuria had become accentuated.

The patient came under the observation of the authors in October, 1938. They record their findings in the blood and in the urine. The patient was put on anti-anaemia treatment, consisting of injections of liver extract and ingestion of syrup of haemoglobin. This was followed on the second night by a violent paroxysm of haemoglobinuria ; the patient became icteric and suffered from lassitude. This aggravation of the haemoglobinuria resulting from stimulation of the haematopoietic tissues suggested a diagnosis of Marchiafava-Micheli disease, and this diagnosis was supported by further findings. The chief points about the case are the early morning haemoglobinuria, the permanent haemosiderinuria, and the fact that the pigment free in the blood was not methaemoglobin but pseudo-methaemoglobin. The red cell resistance was found to be normal, and there was no free haemolysin in the circulating blood. The Donath-Landsteiner reaction was negative. It is noted that the attacks were precipitated by various causes, particularly anti-anaemia treatment. *W. Y.*

ISMAIL (A. A.) & SOLIMAN (M. A.). **Blackwater Fever in Egypt.**—*Jl. Egyptian Med. Assoc.* 1938. July. Vol. 21. No. 7. pp. 394–400.

The authors state that in spite of the prevalence of malaria in Egypt, blackwater fever is distinctly rare. Both benign tertian and malignant tertian malaria are endemic in Egypt, but quartan malaria

is present in certain localities only. The present note describes two cases of blackwater fever occurring in Egyptians who have not left the country.

This is followed by a discussion on the pathogenesis of blackwater fever, in which the following remarkable sentence occurs : " Apparently in Egypt urticaria in malaria takes the place of the much rarer condition, blackwater fever." *W. Y.*

MARSCHALL (F.). Das Schwarzwasserfieber in Santo Domingo. [**Blackwater Fever in Santo Domingo.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1939. June. Vol. 43. No. 6. pp. 266–273. With 1 fig.

In the islands of the Great Antilles, which have a similar origin, the distribution of tropical diseases is very different. In Porto Rico, for example, *Schistosoma mansoni* infections are widespread, whilst in Santo Domingo the parasite is not found. Blackwater fever is common in Haiti and is not uncommon in Jamaica and Santo Domingo, but it is extremely rare in Porto Rico. This is so much the more striking since the inhabitants of these islands belong to the same race, and the climate, soil, fauna and flora are all similar.

Actually blackwater fever in Santo Domingo is not common, about 40–50 cases yearly being recorded. The disease is chiefly found in the western portion of the Republic, bordering on Haiti, and particularly in the districts of Azua, San Juan, and Barahona. In these provinces malaria is also commonly met with.

Clinical details and the post-mortem findings of a case of blackwater are recorded at length. The author then passes to a discussion of four theories which have been advanced to explain the disease, *viz.*, that it is due to a specific organism, such as a spirochaete ; that it is due to a special malaria parasite which exhibits a particularly powerful haemolytic action ; that it is the consequence of a sensitization to particular drugs (quinine) resulting from malaria ; and that it belongs to the allergic or anaphylactic reactions. After discussing these various hypotheses at some length, the author concludes that the last is probably correct. *W. Y.*

FOY (Henry) & KONDI (Athena). **Spleen Puncture Findings in Blackwater Fever.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1938. Nov. 26. Vol. 32. No. 3. pp. 347–354.

During the past two years the authors have punctured the spleens of all patients with blackwater fever who have come under their control, and they have correlated their findings with fairly extensive biochemical and biophysical examination of peripheral blood. They have recorded their data in tabular form, and give the following summary of their observations and conclusions :—

" 1. That there is little or no evidence of heavy malaria infection just prior to the onset of the blackwater fever, in the great majority of cases.

" 2. That if the presence of pigment in the spleen may be taken as evidence of recent schizogony, then very few cases of blackwater fever can be said to be suffering from active malaria at the time of the onset of their haemoglobinuria.

" 3. That the absence of pigment in the spleen may either mean that active schizogony was not going on, or that the organism possesses very variable ability to dispose of pigment rapidly.

"4. That in some patients vast amounts of pigment can be found for very long periods after the initial attack of blackwater, whilst in others none or only the barest traces can be found after the lapse of only a few hours from the first passage of black urine.

"5. That the rate at which the spleen disposes of pigment is an extremely variable factor, not dependent upon the time or amount of quinine taken prior to the onset of the blackwater.

"6. That the reticulo-endothelial system would appear to play an important role in this pigment destruction rate.

"7. That the correlation coefficient between the last dose of quinine and the first passage of black urine is so significant (0·87) as to make it appear that there is more than a casual relationship between the two; although quinine is by no means an essential pre-requisite, since blackwater does occur after atebrin, etc.

"8. That there is little difference between peripheral blood examination and spleen puncture so far as parasites are concerned; the latter is a little superior so far as pigment is concerned.

"9. That patients who have been in hospital and have taken a full treatment for malaria with either atebrin or quinine, sometimes go down without any warning with blackwater fever, their bloods and spleens being negative for both parasites and pigment." *W. Y.*

SARCINELLA (Franco). La febbre biliosa emoglobinurica ed i suoi rapporti col chinino e la malaria. [**Blackwater Fever and its Relationship with Quinine and Malaria.**]—*Rass. Sanitaria dell' A.O.I.* Addis Ababa. 1939. July 9. Vol. 1. No. 2. pp. 101–116. [39 refs.]

This is a long discussion of the well-known theories which have been advanced to elucidate the aetiology of blackwater fever. In summing up, the author points to the relationship between malaria and blackwater, even though the malaria be masked or latent, and to the influence of quinine in precipitating the attacks. Blackwater is probably a malarial manifestation in persons who are for some reason predisposed, and quinine acts as the determining factor precisely because it has a specific affinity for the parasites. This affinity is shown by its power of destroying the parasites if given in curative doses, but if given in small doses to subjects infected with parasites particularly resistant, it may act as a stimulant to those parasites after the manner of salvarsan on spirochaetes. In other words, blackwater fever may be the result of a specific exciting action of quinine on the parasites, at a certain point in the course of malaria in some instances, but the author does not claim that this theory covers all cases.

Three cases are described in detail and a fourth is referred to, but no experimental proof is offered in support of the author's theory.

[For a full account of the history and theories of causation of blackwater fever, the reader is referred to SCOTT, A History of Tropical Medicine, pp. 258–75, see this *Bulletin*, 1939, Vol. 36, p. 791.]

C. W.

THOMAS (Rufus C.) & MILLEN (Robinson M.). **A Case of Pregnancy complicated by Blackwater Fever and** *Bacillus coli* **Pyelitis.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1939. Apr. 6. Vol. 32. No. 6. pp. 743–750.

Details are given of a case of pregnancy complicated by blackwater fever and *Bact. coli* pyelitis. The patient was a missionary's wife

who had returned to Great Britain from the Congo six weeks previously. She had had several attacks of malaria in the Congo and at least one attack of dark-coloured urine, which she had attributed to quinine; she had not taken quinine regularly as it upset her. On the 21st May, 1938, she was admitted to hospital with a diagnosis of accidental haemorrhage. She stated that she had had an attack of malaria the previous day, for which she had taken 10 grs. of quinine. She was at that time in the 36th week of pregnancy. When seen by the authors she was suffering from a typical attack of blackwater fever.

Attention is drawn to the apparent rarity of the occurrence of blackwater fever in pregnant women; and it is suggested as an explanation of this that there may be, in the blood of pregnant women, an increase of haemolytic bodies [presumably a misprint for anti-haemolytic bodies] of sufficient amount to prevent the development of blackwater fever. [See GUNTHER below.] *W. Y.*

GUNTHER (Carl E. M.). **Blackwater Fever following the Administration of "Atebrin."**—*Med. Jl. Australia.* 1938. Dec. 31. 25th Year. Vol. 2. No. 27. pp. 1119–1121.

The author has collected from the literature a number of records of blackwater fever following the administration of atebrin. He also gives details of a case encountered by himself. The patient had apparently been under the author's observation since 1935. Her last attack of malaria was in November 1935, when she was treated successfully with quinine. On July 27th, 1938, she again consulted the author. At this time she was in the fourth month of pregnancy, and she was feeling fit and well, but the spleen extended four fingers below the costal margin. She had had only three prophylactic doses of quinine during the previous ten days, the last being on July 21st. The author ordered a course of atebrin, 0·1 gm. thrice daily for five days. She had one dose on July 28th and three doses on July 29th, but forgot to take her morning dose on July 30th. At 11 a.m. on that day she had a severe rigor and passed blackwater. *W. Y.*

LAFFERRE. Fièvre bilieuse hémoglobinurique observée en France, révélatrice d'un paludisme à "Falciparum." Ankylostomiase. [**A Case of Blackwater Fever observed in France in a Patient with Malaria and Ankylostomiasis.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1938. Dec. 12. 54th Year. 3rd Ser. No. 33. pp. 1700–1702.

Clinical details are given of a case of blackwater fever. After recovery, the patient had a relapse of malaria and *P. falciparum* was found in the blood. The stools contained hookworm eggs. *W. Y.*

CALCUTTA: ANNUAL REPORT OF THE ALL-INDIA INSTITUTE OF HYGIENE AND PUBLIC HEALTH, 1937 [LAL (R. B.), Director].—[**Blackwater Fever** pp. 23–24] [KRISHNAN (K. V.)].

In the previous year's report the author has drawn attention to certain changes in the blood and tissues met with in blackwater fever, and also in malarial haemoglobinuria in monkeys. These changes include focal necrosis of the liver, degeneration of the adrenal cortex, an excessive production of unsaturated fatty acids, a lowering of free-cholesterol and a hypofunction of the reticulo-endothelial system.

Attempts were made to correct these pathological changes and to see how far they would influence the incidence of haemoglobinuria. Treatment of monkeys with glucose, ascorbic acid and cortin gave fairly satisfactory results [this *Bulletin*, 1938, Vol. 35, p. 479].

During the present year this line of treatment has been extended to human beings, and seven cases of blackwater fever were treated in this manner. The cortical extract used was either a commercial preparation obtained from the Wilson Laboratories in Chicago or an extract prepared by the author, following the technique of Swingle and Pfiffner. Both extracts are stated to have given equally encouraging results. The dose used was 1 cc. of the extract (equivalent to 0·1 gm. of fresh gland tissue) twice a day or oftener for about 3 to 5 days. Ascorbic acid was administered in 100 mgm. doses twice daily; glucose was administered intravenously, one pint of a 5 per cent. solution being given twice daily. The author states that in addition all febrile cases and those showing malaria parasites were given atebrin.

It is claimed that this line of treatment led to the following beneficial results :—

" (*a*) A marked diminution in the intensity of haemoglobinuria. The urine cleared up within one to three days.

" (*b*) An increase in the quantity of urine passed. Anuria, if present, was overcome.

" (*c*) Rapid recovery from collapse that is invariably present and improvement in the general condition of the patient; these changes were noticed within 24 hours of the commencement of the treatment.

" (*d*) Complete recovery of all the seven cases treated."

[Much further evidence will be required to convince the reviewer that these results represent a *propter hoc* and not merely a *post hoc* phenomenon.] *W. Y.*

CHOLERA.

Précis of Abstracts in this Section.

The Eastern Bureau of the League of Nations (p. 892) reports that cholera in the East was generally more than usually severe in 1937–1938. Airports must be regarded as foci of spread. The criterion for notification still remains the clinical one. The question of the El Tor vibrio is discussed. There is no general agreement on the question of the value of prophylactic inoculation.

Robertson and Pollitzer (p. 893) consider that cholera during the last few years has been transported to Shanghai from the valley of the river Yuan, partly because agglutinable vibrios identical with true *V. cholerae* have been isolated from the river water. The water is contaminated from junks and in the process of transporting human night-soil for the use of farmers. Flies play a part in transmission. In control vaccination was used and chlorine to 0·9 p.p.m. was added to the buckets of the water carriers. In transfusion proper sterilization must be ensured and bicarbonate of soda may be added in cases of starvation acidosis in undernourished subjects.

READ (p. 894) has found Wilson and Blair's bismuth sulphite enrichment medium to give the best results in the laboratory in the differential isolation of *V. cholerae*, and suggests a field trial.

READ *et al* (p. 895) show that both salt and organic matter are necessary for multiplication and survival of the cholera vibrio and that the presence of other organisms in equal quantity does not prevent multiplication and survival for a time.

BOSE (p. 895) found that the maximum growth of *V. cholerae* on papain-mutton agar occurs in medium in which the papain digestion is continued for 2 hours.

Of 100 strains isolated during the 1938 epidemic in Shanghai, FOURNIER (p. 895) shows that all were of Heiberg's group 1, all gave positive cholera red and negative Voges-Proskauer reaction, and 74 were non-haemolytic from the outset. The majority, 93, were of the intermediate Hikojima type.

Certain changes in morphology, metabolic activity and chemical type were found in *V. cholerae* passed through flies by LAL *et al.* (p. 896), but fermentation and serological reactions were not altered.

RAYNAL *et al.* (p. 896) have obtained a trichloracetic acid extract from *V. cholerae* which precipitates with anticholera serum, is toxic and antigenic and gives allergic reactions in guineapigs sensitized to cholera.

CHECCACCI (p. 897) uses this extract for the preparation of a rabbit anti-serum with which the cholera vibrio may be identified.

SEAL and MITRA (p. 897) have investigated the oxidation-reduction potentials of *V. cholerae.*

At the Pasteur Institute, Shillong (p. 897) attempts at transformation of cholera vibrios failed. Vibrios were almost universally found in natural water sources, but were never agglutinable.

KOESOEMADILAGA (p. 898) shows that subpassage in white mice was only possible with *V. cholerae* if blood plate cultures were interposed between every two animal passages. Intraperitoneal injection was not successful, but may be so if the El Tor vibrio is used. Blood infection may result for a period of a few hours after intraperitoneal injection or feeding with an emulsion of *V. cholerae.* Intestinal infections took place later than blood infections.

GOYLE (p. 898) advises that tests for haemolysin should be applied after incubation for 24 hours instead of for 3 days, as is usually recommended. Red cells from different animals vary in sensitivity, the haemolysin is destroyed by heating and typical cholera immune serum does not neutralize haemolysin though anti-haemolysin sera, which are all homologous, do so.

BEEUWKES (p. 899) contends that the ferments of *V. cholerae* which cause haemodigestion and the liquefaction of gelatin are separate. Haemodigestive power is lost by the El Tor vibrio if cultured on egg medium.

OTTEN (p. 899) points out that the El Tor vibrio is distinguished from *V. cholerae* not only by its haemolytic activity but because it occurs chiefly in persons with symptoms of dysentery, in apparently healthy persons and in isolated cases. Investigating the so-called *V. celebes*, he shows that tests of haemolytic power should be, as they are not yet, carried out according to a standard method, and gives his findings. It remains to be decided whether the Celebes strain is a weakly haemolytic El Tor vibrio, a strongly haemolytic cholera vibrio, or an independent intermediate species.

MAITRA (p. 900) found that the test of inhibition of choleraphages by vibrio extracts, with the precipitin reaction, furnishes two main groups, (1) smooth cholera vibrios and the El Tor, and (2) a heterogeneous group of water and other vibrios.

MERTENS and MOCHTAR (p. 901) demonstrated the want of serological unity in 32 strains of vibrios of various types.

BOSE (p. 901) uses an extract of crude mannose prepared from ivory nut shavings.

BANERJEE (p. 901) gives details of the pathological appearances in cholera, noting the almost constant enlargement of the thymus and degenerative processes in the suprarenal cortex. The clinical type showing renal failure may be due to hypochloraemia rather than dehydration, and the " vasomotor failure type " is regarded as having an allergic basis, which results in increased permeability of intestinal vessels. He suggests that histamine may be absorbed from the intestine, causing the profound fall in blood pressure.

CHATTERJEE (p. 902) from post-mortem examination finds that in cholera there is surprisingly little inflammatory change in the intestines, being marked in only 30 per cent. He describes the changes in various organs and the bone marrow, in which eosinophils amount to 15–20 per cent.

PASRICHA *et al.* (p. 902) investigated the serum reactions of cholera patients. Agglutinins develop about the 4th day and increase, H being earlier and stronger than O. They act best on the homologous strain but act also on standard Inaba strain, not on inagglutinable strains. The serological test may therefore help considerably in diagnosis.

POLEFF (p. 903) describes a method for using agglutinating serum on suspected cholera stools themselves.

PASRICHA *et al.* (p. 903) compared 5 treatments applied to patients in strictly serial order and conclude that choleraphage gave encouraging results, justifying its use as a routine measure.

The epidemic of 1937–1938 in Indo-China was introduced from China. GENEVRAY (p. 904) reports that vaccination was performed on 13,513,350 persons, usually as a single dose. This was efficacious. The vibrios were of the epidemic cholera type and when freshly isolated could grow in 8 per cent. sodium chloride.

GENEVRAY *et al.* (p. 904) describe an epidemic in a village in the Tonking delta. Its origin was obscure but vibrios of the Inaba type were found in two ponds. Vaccination was carried out extensively and to this the authors attribute the sudden end of the epidemic which occurred.

VOGEL and RIOU (p. 905) however, have examined the results of vaccination in Tonking and see no advantage in it. Cholera may disappear spontaneously and may attack vaccinated and non-vaccinated communities indiscriminately, with little difference in mortality.

C. W.

LEAGUE OF NATIONS. HEALTH ORGANISATION. EASTERN BUREAU, SINGAPORE. ANNUAL REPORT FOR 1938. [**Disease Incidence. Cholera in Countries & Ports.** pp. 27–60. With 20 graphs & 5 maps. [18 refs.]]

Under the heading " Cholera in Countries " it is noted that " cholera in British India has been more severe than the average for the preceding quinquennial period." Cholera in the East generally during

1937 and 1938 seems to have been more than usually severe. In China and French Indo-China it is understandable that the refugee influx into certain territories would be a powerful factor in epidemicity.

As in the case of plague airports must be added to seaports as foci of special, or even greater danger for the spread of cholera. Notifications from airports in British India were received from Allahabad, Cawnpore, Delhi and Jodhpur, from Hanoi in French Indo-China and from Hankow in China. Calcutta among the seaports is credited with having been infected, as usual, with cholera throughout the year. In connexion with this statement of unenviable invariability for the Hoogly Delta it is interesting to learn that the Commissioner in charge of League of Nations Anti-Epidemic Unit 2 suggests " that cholera in Central China is endemic."

Many interesting points are raised in this report which are also of the highest importance: " The Cholera Commission considered that the criterion to be adopted in notifying proved cases of cholera under the 1926 Convention still remained the clinical one," while " at a subsequent meeting the Commission expressed the opinion that from the point of view of the sanitary measures to be taken neither the El Tor nor the non-agglutinable vibrios can be considered as comparable to the cholera vibrio of Koch." This reference to the El Tor question occurs in the report in a commentary at the end of the paragraph on " Cholera in Netherlands India." It has reference to what, it has been suggested, should be called *Vibrio celebes*, regarded as an El Tor type, although with somewhat ill defined characters. A map is also given showing location of " El Tor " cases in Celebes. [See this *Bulletin*, 1939, Vol. 36, pp. 374, 375.]

Another indirect reference to El Tor is the quotation of the view of DOORENBOS on the factors favouring the conservation and regeneration of the cholera vibrio. " It has been found at Tor that while vibrios often disappear spontaneously from healthy carriers, such is not the case with those carriers who are suffering from dysentery."

Prophylactic inoculation against cholera comes in for a somewhat mixed treatment. " Discussions on this point which took place at the meeting of the Advisory Council of the Eastern Bureau at Hanoi and subsequently . . . showed that no unanimity existed in regard to its value during an epidemic " or to quote from opinions nearer home: " TOPLEY and WILSON refer to the difficulty in assessing the value of cholera inoculation in reports which have been published." POLLITZER working in the midst of epidemic cholera in China "refers to the distrust which some observers have of statistics tending to prove the value of anti-cholera vaccination and suggests that what is needed is discrimination in regard to statistical evidence rather than general scepticism." Exact interpretation of his opinion would depend largely on the meaning conveyed by the word " discrimination."

W. F. Harvey.

ROBERTSON (R. Cecil) & POLLITZER (Robert). **Cholera in Central China during 1938 - its Epidemiology and Control.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1939. July 28. Vol. 33. No. 2. pp. 213–232. With 1 map & 17 figs. on 4 plates.

An account is given of the working of the English-speaking second unit of the League of Nations Epidemic Commission to China in the provinces of Hunan, Hupeh and Kiangsi, during 1938, which was a

year of epidemic cholera intensified by war conditions. Every endeavour was made, and evidently successfully, to co-operate with the Chinese health services, both civil and military. It had been suspected that cholera during the last few years had been transported to Shanghai from an unknown endemic focus in the mid-Yangtse basin. This focus has been now identified as probably the valley of the Yuan, a river which flows into the Yangtse through the Tung-ting lake. One of the important pieces of evidence on this point was the ability to isolate agglutinable vibrios identical with true *V. cholera* from the river water itself. One of the sources of contamination of river water was the habit of urination and defaecation by crews of junks into the river and also the practice of careful collection of human night soil in barges, for " export to farmers in rural areas." Not that the barges themselves leaked to any serious extent ; the danger of cholera infection of the river lay rather in the habit of washing night soil containers in the river after being emptied into the barges.

Modes of infection to be considered were infection by contact, by flies, by food and by water. It is contended that (1) contact infection was of no importance ; (2) transmission by flies " plays a considerable part " ; (3) the end of the water melon season was coincident with a decline in cholera but the water melon is only contaminated by flies and by watering of the cut surfaces with polluted water ; (4) polluted water was the chief source of infection. It seems improbable, however, that infection travelled by river water for any considerable distance. In fact cholera often spread upstream rather than downstream.

Protective inoculation was undertaken and seems to have been well received. In the dose used, a single dose of 6,000 million per cc., there was never any general reaction and the local reaction was slight. Some attempts were made to use simple methods of safeguarding water supplies. It did not seem politic, however, to try and interfere with the disposal of night soil. One of the methods used was to add 0·25 per cent. chlorine solution by means of measuring bamboo cups to the individual buckets of water-carriers. The concentration of chlorine worked out to 0·9 p.p.m.

The points emphasized by the medical workers in employing transfusion for cholera cases were the use of a properly sterilized distilled water for normal and hypertonic salt solutions and the recommendation of bicarbonate of soda in the transfusion solution for ill-nourished patients suffering from a starvation acidosis. *W. F. H.*

READ (W. D. B.). **Differential Isolation of** *V. cholerae.—Indian Jl. Med. Res.* 1939. Apr. Vol. 26. No. 4. pp. 851–865.

It has been found by experience that the alkaline peptone water used for enrichment in the isolation of vibrios from water and stools is apt to allow growth of many organisms which are prejudicial to their growth. The subsequent use of a solid medium, such as that of Aronson, is apt to be rendered nugatory because the vibrios sought for have been already overgrown. One of the difficulties to be surmounted is the maintenance of the reaction of the enrichment medium and it is absolutely necessary, by stoppering, to prevent spontaneous fall of *p*H with the absorption of carbon dioxide from the air. Another useful device was the addition, during incubation, of small quantities of alkali to restore the *p*H [see also this *Bulletin*, 1939, Vol. 36, p. 378].

So far as these laboratory experiments go the best results in the differential isolation of *V. cholerae* were obtained with a modification of WILSON and BLAIR's bismuth sulphite enrichment medium and this medium will now require to be tested in the field. It is evidently desirable to obtain "a carbohydrate specifically fermented by *V. cholerae*," in order to make certain of the isolation of this vibrio. *W. F. H.*

READ (W. D. B.), SINGH (Gurkirpal), SEAL (S. C.) & BOSE (S.). **Growth and Survival of *V. cholerae*, with Special Reference to Growth and Survival in Water.**—*Indian Jl. Med. Res.* 1939. July. Vol. 27. No. 1. pp. 1–40. With 1 graph. [18 refs.]

Many experiments have been done on the survival of cholera vibrios in water. Few of these have concerned themselves directly with the question of multiplication of vibrios as distinct from survival. It is interesting therefore to find from the authors' experiments that "the conditions for multiplication and survival are very similar." The conditions studied were: Salt concentration, organic matter content, *p*H, size of vibrio inoculum and the action of other organisms commonly present in water and stools. It is shown that:—(1) Both salt and organic matter are necessary for multiplication and survival of the cholera vibrio in artificial water but that the amount of salt required decreases with increase of concentration of organic matter. (2) The presence of other organisms in comparatively equal inocula . . . does not seem to prevent the multiplication and survival of *V. cholerae* up to 5 days or longer. In the presence of the inagglutinable vibrio the agglutinable vibrio can survive up to 3 weeks or longer.

The details of experimentation are given in 12 tables. *W. F. H.*

BOSE (Sarashipada). **The Nutritive Value of Papain-Mutton Broth.**—*Indian Jl. Med. Res.* 1939. July. Vol. 27. No. 1. pp. 65–71. [15 refs.]

Papain digests protein only to the stage of peptone. Although papain is a true protease it can only split peptone when activated by hydrocyanic acid and consequently a papain digest medium cannot contain free amino-acid. It is essential in the use of the cheap papain mutton medium to determine the optimum conditions for complete digestion. Progress of digestion of mutton was determined by estimations of amino-nitrogen by formol titration, oxidizable matter and total nitrogen at intervals of ½, 1, 2, 3, 4, 5 and 6 hours. Thus digestion of 300 gm. mutton with 5 gm. papain was found to be complete in 2 hours at 60°C. It was also found that the maximum growth of the cholera vibrio on papain-mutton agar at different stages of digestion was obtained after 2 hours' digestion. *W. F. H.*

FOURNIER (J.). Type sérologique des vibrions isolés à Changhai pendant l'épidémie de 1938. [**Serological Type of Cholera Vibrios at Shanghai. 1938.**]—*Bull. Office Internat. d'Hyg. Publique.* 1939. June. Vol. 31. No. 6. pp. 1041–1043.

In the cholera epidemic of 1938 which raged in Shanghai from May to October, 1,107 vibrio strains were isolated from hospital patients. These were sealed for further study. A selection of 100 of those strains was made which had been derived from the most typical cholera cases, presented typical biochemical character and had shown a titre of at

least 1/5,000 after 2 hours at 37°C. with the laboratory serum. All were found to belong to Heiberg's group I (mannose and saccharose positive, arabinose negative); all gave a positive cholera red and a negative Voges-Proskauer reaction. Out of the 100 strains 74 were non-haemolytic from the outset and 26 had shown some degree of haemolytic action on suspensions of sheep erythrocytes. Any haemolytic property possessed by freshly isolated strains was lost after some months. Each of the strains was tested serologically after saturation of an Inaba, Hikojima and Ogawa serum by the heterologous type organisms, and showed that 4, 93 and 2 strains were original Inaba, intermediate Hikojima, and variant Ogawa respectively. One strain was unclassifiable. This confirms the finding for the epidemic of 1933, where also the intermediate type of vibrio was highly preponderant.

W. F. H.

LAL (R. B.), GHOSAL (S. C.) & MUKHERJI (B.). **Investigations on the Variation of Vibrios in the House Fly.**—*Indian Jl. Med. Res.* 1939. Jan. Vol. 26. No. 3. pp. 597–609.

These investigations were undertaken in order to determine whether changes occurred in cholera vibrios after passage through flies, such as might give colour to the view that they existed in a form which was not readily recognizable in an endemic region or in an inter-epidemic period. "From the epidemiological point of view this matter is of considerable importance." Great precautions were taken to breed out flies which could be said to be free from infections. This much was certainly effected: "The insects were invariably found to be free from contamination with bacteriophage or with organisms even remotely resembling *V. cholerae.*"

The experiments have, on the whole, been indecisive and "no conclusions have, therefore, been drawn at this stage." The results may be summarized :—(1) Certain changes are described in the morphology of the vibrios and their colonies but no change in fermentation reactions and no change of "O" serological type. (2) "Changes in metabolic activity and in chemical type as determined by the methods employed by LINTON . . . were found in the case of many of the strains recovered from flies."

W. F. H.

RAYNAL (J.), LIEOU (Y. Ch.) & FEISSOLLE (L.). Propriétés biologiques d'un extrait trichloracétique (antigène complet) obtenu à partir du vibrion cholérique. [**Biological Characters of a Trichloracetic Cholera Extract.**]—*Rev. d'Immunologie.* Paris. 1939. July. Vol. 5. No. 4. pp. 317–320.

Previous work had shown that a complex unstable compound consisting of polysaccharide and phospho-fatty acid could be extracted with trichloracetic acid from many gram-negative bacteria. BOIVIN and MESROBEANU consider that this represents both endotoxin and somatic antigen. The same technique of extraction has been followed by the authors in the case of the cholera vibrio and a pale yellow liquid obtained. It possesses precipitating action on anticholera serum, toxic action on mouse and rabbit, antigenic and immunizing power in the rabbit and intradermic allergic action in guineapigs sensitized intraperitoneally with living cholera vibrios. [See also *Bulletin of Hygiene,* 1938, Vol. 13, p. 748, and 1937, Vol. 12, p. 379.]

W. F. H.

CHECCACCI (L.). Ricerche sulla struttura antigene del vibrione colerigeno. Nota I. Studio del cosidetto antigene glucido-lipidico in rapporto alla classificazione di Gardner e Venkatraman. [**Antigenic Structure of the Cholera Vibrio. Glyco-lipoid Antigenic Constitution and Classification.**]—*Boll. Istituto Sieroterap. Milanese.* 1939. June. Vol. 18. No. 6. pp. 391–407. [75 refs.] German summary.

BOIVIN and MESROBEANU's method of obtaining a soluble extract of cholera vibrios by means of trichloracetic acid has been followed and the object of this research is the elucidation of the antigenic properties of this complex phospho-fatty compound with polysaccharide. It has, in all probability, been identified with the specific O antigen which forms the basis of the classification of vibrios into subgroups by GARDNER and VENKATRAMAN. Intravenous inoculation of the extract in the rabbit produces a serum which specifically agglutinates and precipitates homologous vibrios in high titre and fails to agglutinate, except in low titre, vibrios belonging to other serological subgroups and the cholera-like vibrios. It is usable for the identification of the cholera vibrio in the same way as an O serum, with this difference, that it manifests its specificity either towards living vibrios or to vibrios killed at 100°C. for two hours. *W. F. H.*

SEAL (S. C.) & MITRA (B. N.). **Oxidation-Reduction Potentials of *Vibrio cholerae* and Related Organisms.**—*Indian Jl. Med. Res.* 1939. Jan. Vol. 26. No. 3. pp. 625–630. With 2 graphs & 1 plate.

An elaborate combined potentiometer and *p*H meter was used. It was found that "the average potential curves of the organisms belonging to different chemical groups were . . . different from one another." The *p*H values follow very closely the fall and rise of electrode potential curves. These curves, under the conditions of experiment, show a fall to a minimum in about 6 hours and then a gradual rise to a maximum in about 30 hours. The fall "corresponds to the so-called lag phase of the growth of the organisms and is characterized by having low *p*H in the medium." *W. F. H.*

SHILLONG: KING EDWARD VII MEMORIAL PASTEUR INSTITUTE AND MEDICAL RESEARCH INSTITUTE. TWENTY-FIRST ANNUAL REPORT FOR YEAR ENDING 31ST DECEMBER, 1937 [AHUJA (M. L.), Director]. pp. 6–10.—**Cholera Enquiry under the Indian Research Fund Association.**

With the closure of the Field Unit at Habiganj in 1937, cholera enquiry at the Institute has been directed to purely laboratory research. These researches are given in some detail and some of them have been already published. Attempts at transformation of agglutinable cholera vibrios to inagglutinable forms are a fertile subject of research and an endeavour was made to change the Inaba rough strain to the Rangoon "Rough," which is a smooth but non-agglutinable vibrio of a different type, often isolated from cases of cholera. The experiment failed. Other experiments on transformation were directed to keeping an agglutinable vibrio in raw water but the evidence that it changed into an inagglutinable vibrio was quite unconvincing. "The duration of life of the inagglutinable vibrio as such was short, the maximum period of life being 7 days."

Enquiry into the incidence and characters of vibrios in natural water sources extended to 77 samples, 54 from tanks and 23 from rivers. These yielded 21 organisms of which 2, 2, 7 and 10 were placed in HEIBERG's groups I, II, III and IV respectively. No example of groups V and VI were isolated. Study along these lines showed that "vibrios are almost universally present in natural water sources" but that "in no instance was an agglutinable vibrio isolated."

Publication of the work on papain-casein medium as a substitute for papain digest mutton in the propagation of bacteriophage has already been abstracted [this *Bulletin*, 1939, Vol. 36, p. 377]. *W. F. H.*

KOESOEMADILAGA (R. M. R.). Experimenteele cholerainfectie bij witte muizen. [**Experimental Cholera Infection in White Mice.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1939. June 27. Vol. 79. No. 26. pp. 1602–1622. [16 refs.]

Much argument has centred around the question whether cholera vibrios are to be found in the blood stream, for a time at least, and whether they thus reach the internal organs. Most of the earlier trials negatived this occurrence and it was only later that SANARELLI especially put forward the contention of entry of the cholera vibrio via the faucial ring of lymphoid tissue into the lymphatic and then the blood stream. His contention was that the acidity of the gastric juice and the gastric mucosa constituted an almost absolute barrier to passage of the cholera vibrio. The enterotropic character of the cholera organism was pronounced and independent of the mode of administration, whether oral, subcutaneous, intraperitoneal or intravenous. The present author in his own experiments, which are purely animal, has made a departure from custom in using white mice as test animals and he has found them perfectly suitable. He introduced vibrio suspensions by tube into the stomach, placed culture material on the tongue and fed his animals with bread soaked in a suspension of vibrios. The results are given with a certain amount of caution, owing to the small number of animals used. He has shown that :—(1) White mice are suitable animals for testing cholera vibrios. (2) Subpassage was proved possible from animal to animal with the El Tor but not with either of the two cholera strains used. Continuity of passage could, however, be attained with cholera also if a blood plate culture was interposed between every two animal passages. Subpassage was made from the spleen of the animal. (3) Intraperitoneal injection of El Tor vibrios, after they had been passaged 5 times, killed 18 of 30 animals within 24 hours : cholera vibrio injection was without result, except in one case, for 20 animals. (4) Intraperitoneal injection of vibrios and feeding with vibrio suspension gave rise to blood infection in 10 minutes and disappearance again after 6 to 10 hours. No general blood infection followed deposition of culture on the tongue or feeding with soaked bread. (5) Intestinal infections took place later than blood infection. *W. F. H.*

GOYLE (Amar Nath). **Observations on Haemolysis by Vibrios.**—*Indian Jl. Med. Res.* 1939. Jan. Vol. 26. No. 3. pp. 611–624.

The vibrio strains tested were all of haemolytic type and their potency as regards production of haemolysin was determined after 2 and 4 hours incubation and thereafter daily up to 10 days. Some

interesting variations of potency were manifest in this series, but all the strains showed some degree of haemolytic power after 4 hours. Continued incubation might show diminution of potency and this leads to the conclusion that tests for haemolysin should be applied after 24 hours incubation and not—as is usually recommended—after 3 days. A number of interesting features were determined for the vibrio haemolysin by the quantitative experiments of the author such as, that :—(1) erythrocytes of different species of animals show varying sensitiveness to haemolysin, greatest in the guineapig, about the same in goat, sheep and rabbit and least in pigeon, monkey, horse and man. No correlation could be found between cholesterol or lecithin content and haemolytic sensitivity. (2) The haemolysin was filterable in spite of some adsorption in the process. It is completely destroyed in 10 minutes at 56°C. and the potency of cultures or filtrates is lost if kept at 37°C. Cold storage preserves haemolysin with or without the addition of 0·5 per cent. phenol. (3) Anti-haemolysin sera appeared all to be neutralizing and of homologous nature, but a "typical cholera vibrio immune serum failed to show any neutralizing action." *W. F. H.*

BEEUWKES (H.). Ueber die proteolytischen Fermente des Vibrio cholerae und des Vibrio El Tor. [**The Proteolytic Ferments of the Cholera and El Tor Vibrios.**]—*Zent. f. Bakt.* I. Abt. Orig. 1939. Feb. 20. Vol. 143. No. 3/4. pp. 220–225. With 2 figs. [10 refs.]

The property possessed by the cholera vibrio of haemodigestion, where a green transparent sharply defined zone develops around colonies, and the property of liquefying gelatin have a certain parallelism, which might signify that they were due to one and the same ferment. It has been objected to this view that the properties of all ferments may be influenced by much the same factors and that a parallelism of variation does not justify the conclusion as to identity. The author himself contends that the two ferments are distinct and uses two different cholera strains for a demonstration that they did not individually behave according to expectation in their action on gelatin and on blood, as they should have done if the ferments concerned were identical.

In the same research 4 El Tor strains were investigated for their haemodigestive and gelatin-liquefying characters. The strains were subcultured on agar and preserved on a special egg medium. Liquefying power was estimated by means of the viscosimeter. It was found that the El Tor strains cultured on blood agar exhibited greater liquefying and digesting power than was the case with strains kept on the egg medium. On this latter medium haemodigestive power was lost. *W. F. H.*

i. OTTEN (L.). Het cholera-El Tor-probleem. [**The Cholera-El Tor Problem.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1939. Mar. 14. Vol. 79. No. 11. pp. 642–654. [46 refs.]

ii. ——. **The Cholera-El Tor Problem.**—*Meded. Dienst d. Volksgezondheid in Nederl.-Indië.* 1939. Vol. 28. No. 1. pp. 13–21. [46 refs.]

i. The El Tor vibrio problem has been raised anew with the isolation in a small epidemic by DE MOOR of a haemolytic vibrio. In this

epidemic the patients all had typical cholera symptoms. Now it has to be remembered that the original El Tor vibrio, although morphologically and serologically identical with the cholera vibrio, makes its appearance for the most part in individuals with symptoms of dysentery, in apparently healthy individuals and in the sporadic non-epidemic cholera case. These are features pertaining to the El Tor vibrio, as well as its haemolytic activity, which so far distinguish it from the cholera vibrio. The epidemic in question occurred on the island of Celebes and the vibrio isolated has been named provisionally *V. celebes*. Otten has examined the characters of this organism in detail and has looked closely into the technique for proving a vibrio to be haemolytic. It is remarkable that the technique for establishing haemolytic character differs rather widely in different hands. Otten has investigated such points as age of bouillon culture, duration of incubation for the production of haemolysis and mode of addition of the testing blood. His conclusions are :—

1. (*a*) The Celebes strains show haemolysis constantly within 24 hours although much more weakly than the typical V. El Tor ; the formed haemolysin is more labile and is absent from 5-day bouillon cultures. (*b*) This haemolysis is not demonstrable in 3-day bouillon cultures or in 2–day peptone water cultures when culture and blood are incubated together for only 2 hours at 37°C.

2. (*a*) These phenomena may, however, be exhibited even by cholera strains, although not regularly and much more weakly than by the Celebes strains ; the formed cholera haemolysin is even still more labile. (*b*) No haemolysis occurred, however, in cholera bouillon cultures even after continuous incubation at 37°C., if the added blood was first allowed to sink before inoculating the culture.

3. It is very desirable that the haemolysis test should be carried out according to a standard method.

It remains to decide whether the Celebes strain is to be regarded as a weakly haemolytic El Tor vibrio, a strongly haemolytic cholera vibrio, or an independent species with a position intermediate between the other two.

ii. This is a version of the above written in English. *W. F. H.*

MAITRA (N. M.). **On Inhibition of Individual Types of Cholera-Bacteriophage by Vibrio Extracts.**—*Indian Jl. Med. Res.* 1939. July. Vol. 27. No. 1. pp. 41–49.

It has been shown previously that extracts of typical cholera and allied vibrios were capable of inhibiting choleraphage lytic action and that 3 groups of these vibrio strains could be differentiated by the application of these inhibition tests. The present work continues this study and combines it with precipitin reactions. According to previous work it was also found that phage inactivating power " is destroyed by the addition of homologous antiserum concurrently with the appearance of specific precipitin reaction." The work now undertaken shows that : (1) The test of inhibition of choleraphages by vibrio extracts, together with the precipitin reaction of these extracts, furnishes two main groups : (*a*) typical smooth cholera vibrios and the El Tor vibrios belonging to " O " subgroup I, (*b*) a heterogeneous group of water and other vibrios. The inhibition and precipitin reactions would seem to depend on a common factor related

to the complex polysaccharide receptor of the cholera vibrio but not to the polysaccharide type as determined by chemical analysis.

W. F. H.

MERTENS (W. K.) & MOCHTAR (A.). **An Investigation of Vibrios in the Netherlands East-Indies.**—*Indian Jl. Med. Res.* 1939. July. Vol. 27. No. 1. pp. 51–63. [13 refs.]

Out of 510 vibrio strains isolated from 20,444 samples of faeces and water, 32 were found to agglutinate with an HO cholera serum. These 32 strains were represented by 15 from non-cholera patients, 16 from healthy stools and 1 from water. They formed along with 10 cholera and 10 El Tor and *V. celebes* control strains the material for study. Special anti-sera were made to individual strains and it was found that 17 such sera were still insufficient to classify the 32 strains, thus indicating their want of serological unity. The conclusions were also reached that anti-O cholera sera are more specifically diagnostic than OH sera and that HEIBERG's fermentative classification is insufficient if used alone. *W. F. H.*

BOSE (Sarashipada). **Note on the Preparation of an Unpurified Mannose Solution for Bacteriological Use.**—*Indian Jl. Med. Res.* 1939. July. Vol. 27. No. 1. pp. 73–74.

Mannose, a very expensive sugar, is invaluable for the classification of vibrios by fermentation methods. The author has obtained an extract of crude mannose from ivory nut shavings—a waste product in button manufacture—which gives the same fermentation results as the pure sugar. Three pounds of ivory nut shavings treated by the method described yielded 620 gm. mannose. *W. F. H.*

BANERJEE (Dhirendra Nath). **Outlines of the Pathology of Cholera.**—*Jl. Indian Med. Assoc.* 1939. Apr. Vol. 8. No. 7. pp. 391–395. With 4 figs. on 1 plate. [37 refs.]

The pathological appearances of some of the organs of the body in cholera cases is referred to in useful detail. In the small intestine congestion of both serous and mucous surfaces is a marked feature, but whereas the peritoneal coat used to be described as dry this appearance is now seldom seen, provided the patient is not allowed to die of dehydration. Peyer's patches especially, but also the solitary lymphoid follicles, appear prominent. On microscopic examination the characteristic features in the small intestine are extreme necrotic change in the intestinal epithelium, distension of the capillaries, profound subepithelial oedema and distension of gland tubules with cholera vibrios. It seems probable that the destruction "of the epithelial lining of the small intestine is the cause of the great drain of the body fluid and salts" into the lumen of the intestine. A pathological change which has been almost constantly noted is enlargement of the thymus, possibly because it is a lymphoid organ. On the other hand the spleen is not enlarged and may appear small and wrinkled if death takes place during the stage of dehydration. Reference is made to the pathology of the suprarenals because of the suggested adrenal insufficiency as a factor in the production of the syndrome of cholera. Degenerative changes are to be found in the suprarenal cortex.

On the clinical side two types of cholera are separated out as distinct from what the author calls the straightforward type. These are the "renal failure type" and the "vasomotor failure type." In the renal type it seems possible that hypochloraemia may be of greater importance than simple dehydration [see also this *Bulletin*, 1939, Vol. 36, p. 380]. Under the vasomotor type the author deals with the profuse evacuation in cholera, which is regarded as due to increased permeability of intestinal vessels and, in its mechanism, to be of the nature of gastro-intestinal allergy. Allergy again, but of a bacterial type, is discussed in connexion with the explanation of the algid phase of cholera as due to the conjoined action of extraneous intestinal organisms and the cholera vibrio. A final suggestion is that histamine may be absorbed from the intestine in cholera infection and produce, by its well known toxic dilating action on blood vessels, the profound fall in blood pressure which is seen in cholera. *W. F. H.*

CHATTERJEE (Hemendranath). **A Contribution to the Pathology of Cholera.**—*Jl. Indian Med. Assoc.* 1939. May. Vol. 8. No. 8. pp. 449–454. With 8 figs. on 2 plates. [22 refs.]

Two parts make up this contribution :—i. The gastro-intestinal tract in cholera and ii. Haemolymph organs.

i. In 85 post-mortem cases agglutinable cholera vibrios were cultured, in 70 per cent. from the intestine, 60 per cent. from the gall bladder and 25 per cent. from mesenteric glands. All told 80 per cent. "showed the vibrio from one or more sources." Macroscopic changes in the intestine were : marked in only 30 per cent., slight congestion in 50 and nil in 20 per cent. A dry appearance of the serosa is not now seen and this is due to the use of therapeutic saline infusion. Microscopically the pink velvet colour of the gastro-intestinal tract is not often well represented by capillary congestion, which seems to disappear in fixation of tissues. Surface epithelium may be perfectly intact. Lymphoid follicles are enlarged and may show numerous mitotic figures. It is rather extraordinary that a disease with so violent gastro-intestinal symptoms should show so little inflammatory change. The congestion is mostly non-inflammatory and more or less confined to mucosa and submucosa.

ii. In the dark red bone marrow of the femur there are cavernous capillary blood spaces and a preponderance of eosinophils amounting to 15–20 per cent. compared with 3–6 per cent., which is a very different type of reaction from that of inflammatory toxaemia. The spleen was enlarged in a high proportion of the cholera cases and showed an average weight of 199 gm. compared with 160 gm. The enlargement is mainly congestive. Microscopically the Malpighian bodies are hyperplastic. In other organs and situations vascular dilatation and hyperplasia of lymphoid tissues are the chief features.

W. F. H.

PASRICHA (C. L.), CHATTERJEE (D. N.) & PAUL (B. M.). **H & O Agglutinins in Cholera Patients.**—*Indian Med. Gaz.* 1939. June. Vol. 74. No. 6. pp. 330–334.

Although work has been done on the development of agglutinins in cholera cases this was done before the H and O agglutinins had assumed the importance of the present day. In the present investigation the authors examined 175 patients for their serum reactions,

according to the day of the disease, with H (0·2 per cent. formolized) and O (boiled) suspensions of young agar cultures. The strains used were Inaba and the homologous organism and the results may be summarized as follows :—(1) Agglutinins have usually developed by the 4th day but are more frequent and of higher titre by the 7th day. (2) H agglutinins appear earlier, in greater concentration and more consistently than O agglutinins. (3) Agglutinins are better developed for the homologous strain than for the standard *V. cholerae* (Inaba). (4) Agglutinins when developed acted only on *V. cholerae* and not on inagglutinable strains. (5) As it is not always possible to isolate *V. cholerae*, the serological test can contribute materially to the diagnosis of cholera. *W. F. H.*

POLEFF (L.). Le diagnostic bactériologique rapide du choléra. [**Rapid Bacteriological Diagnosis of Cholera.**]—*Bull. Soc. Path. Exot.* 1939. June 14. Vol. 32. No. 6. pp. 595–597.

In the great war certain procedures were adopted in bacteriological diagnosis which may now once more prove useful. The following is a description of a method by which agglutinating serum is utilized to show specific serum reaction on suspected cholera stools themselves :—

(1) Set up 3 large test tubes containing 10 cc. of the usual peptone water. (2) Add 5 drops of test stool to each of these tubes. (3) Add to two of the tubes agglutinating cholera serum to full titre strength (*e.g.* 1–2000) and to half titre. (4) Keep the third tube as control and, better still, set up a fourth control tube of peptone water containing agglutinating serum and sown with known cholera. (5) Incubate all the tubes at 37°C. (6) Examine for signs of agglutination in 3 to 6 hours or later of proliferating cholera vibrios, evident at the upper surface portion of the tubes.

W. F. H.

PASRICHA (C. L.), DE MONTE (A. J. H.), CHATTERJEE (B. C.) & MIAN (A. Samad). **Treatment of Cholera (a Note on the Results of Treatment by Different Methods).**—*Indian Med. Gaz.* 1939. July. Vol. 74. No. 7. pp. 400–401.

Simultaneous comparison of different methods of treatment applied to patients taken in strictly serial order is an ideal method of arriving at definite conclusions on the value of each method. It has been applied by the authors to 271 cholera patients who "were treated by five different methods during a period of five weeks when the incidence of the disease was high. The methods employed were : (1) divided doses of calomel, (2) potassium permanganate, (3) essential oils, (4) bacteriophage, and (5) M & B 693," in 90, 40, 47, 44 and 50 patients respectively with the uncorrected percentage mortalities of 18·9, 15·0, 10·7, 4·5 and 10·0. Correction of these mortalities consisted in excluding moribund cases, etc., from the several groups but the order of the mortalities remains much the same. It is a little surprising that in so well-planned a trial the deductions made from the results are not very emphatic :—

"The results of choleraphage therapy are striking and are sufficiently encouraging to justify the adoption of bacteriophage as a routine measure in the treatment of cholera and other methods should be compared with the results of bacteriophage therapy."

W. F. H.

GENEVRAY (J.). Le choléra en Indochine en 1937–1938. [**Cholera in Indo-China. 1937–1938.**]—*Bull. Office Internat. d'Hyg. Publique.* 1939. June. Vol. 31. No. 6. pp. 1024–1040. With 1 chart & 1 folding map.

Cholera tends to appear in Indo-China in sharp epidemics with long intervals between. The epidemic of 1926 was the most fatal ever recorded but no cases of cholera have been recorded in Cambodia and Cochin-China since 1934 and in Annam since 1934. Neither Laos nor Tonking have had any cases for 10 years. The present epidemic was introduced from China. Where a country has such an indented coast line and so many creeks, seaport quarantine is almost certain to be ineffective. Water carriage seems to have played but little part in transmission which was from case to case. Although the epidemic was not a severe one in its extent it had a high mortality of 60 to 80 per cent. The symptoms were of ordinary type.

Vaccination measures were applied on a large scale and 13,513,350 vaccinations carried out. Although the majority of these were of the single dose type it is considered that they were efficacious. When full vaccination was carried out, as in the case of administrative and military groups, it gave complete protection from cholera.

Some interesting laboratory investigations were conducted on the vibrios, which appear to have been very uniformly of the epidemic cholera type. The practical superiority of the use of O sera was established. No pseudocholera vibrios were isolated and on only two occasions were cholera vibrios isolated from water. Bacteriophage, however, was isolated from ponds around which cases of cholera had occurred.

It was found that the freshly isolated cholera vibrio is resistant to high concentrations of salt and can grow in an 8 per cent. sodium chloride. A culture medium which utilized this property was tried out with success and with great saving of time and work. [See also this *Bulletin*, 1938, Vol. 35, p. 742, and 1939, Vol. 36, p. 378.]

W. F. H.

GENEVRAY (J.), BRUNEAU (J.) & SEYBERLICH (A.). Etude d'une épidémie de choléra dans un village du delta Tonkinois. [**A Cholera Epidemic in a Tonking Delta Village.**]—*Bull. Soc. Path. Exot.* 1939. Mar. 8. Vol. 32. No. 3. pp. 262–267. With 2 figs.

The interest of this epidemic lay in its sudden occurrence in a small community of not more than 1,200 persons, when no cholera had been notified in the Province for 4½ months and none in the whole of Tonking for 1½ months. It was all over in 15 days but consisted of 60 cases with 52 deaths. The vibrios isolated from the stools in the course of the epidemic were of Inaba type. Other interesting points in connexion with this epidemic were that the only well of the village gave no cholera but vibrios with all the Inaba characters were isolated from two village ponds. Then, also, there were no carriers found among individuals in the households of patients or even among the cured patients themselves ; no trace of bacteriophage could be found to account for the sudden termination of the epidemic or the sudden disappearance of cholera from the village ponds. As 980 vaccinations were performed almost immediately the epidemic broke out, the authors conclude that it was this measure which brought the outbreak to so sudden a finish. *W. F. H.*

VOGEL (E.) & RIOU (M.). Les maladies épidémiques, endémiques et sociales dans les colonies françaises pendant l'année 1937. Choléra. [**Disease in French Colonies in 1937. Cholera.**]—*Ann. de Méd. et de Pharm. Colon.* 1939. Apr. Vol. 37. Supplement. pp. 270–286.

An account of the ravages of cholera in each of the French colonies is given in some detail. It is a little unusual to find a reasoned statement in an official report which is adverse to the almost universal acceptance of the efficacy of vaccination. The medical officer of the province of Namdinh in Tonking, in which 764,500 vaccinations were performed, has seen spontaneous arrest of cholera in non-vaccinated villages and its recrudescence in vaccinated villages. He considers also that epidemic cholera came to an end in non-vaccinated China at the same time as it did in vaccinated Tonking. In the province of Annam little difference in mortality is manifest between vaccinated and non-vaccinated villages, while in the province of Vinh, where cholera ceased in the primary focus after a massive inoculation of the population, it was found that on recurrence it ravaged indifferently vaccinated and unvaccinated villages. A wise remark on vaccination made in this report is that: "It is, however, necessary to be very circumspect in interpreting the results in a favourable as well as an unfavourable sense." *W. F. H.*

JOURNAL OF THE ASSOCIATION OF MEDICAL WOMEN IN INDIA. 1939. May. Vol. 27. No. 2. pp. 145–147. **The Cholera Danger. Useless Vaccines on the Market. Necessity for using Genuine Vaccine.**

There is no doubt of the existence of very numerous cholera-like organisms and much time and care has been devoted to defining the characters of the true cholera vibrio. As there is some possibility that the latest research work on the subject is not known to all purveyors of cholera vaccine, three of the main Government laboratories have undertaken to issue suitable strains to laboratories and commercial firms for the preparation of vaccine. *W. F. H.*

GAUDUCHEAU (A.). La vaccination anticholérique en Indochine. [**Anti-Cholera Vaccination in Indo-China.**]—*Bull. Soc. Path. Exot.* 1939. May 10. Vol. 32. No. 5. pp. 471–473.

CALCUTTA: ANNUAL REPORT OF THE CALCUTTA SCHOOL OF TROPICAL MEDICINE AND THE CARMICHAEL HOSPITAL FOR TROPICAL DISEASES 1938 [CHOPRA (R. N.), Director].—[**Cholera** [DEMONTE (A. J. H.)] pp. 121–132. With 2 charts.]

EPIDEMIC DROPSY AND DEFICIENCY DISEASES.

PRÉCIS OF ABSTRACTS IN THIS SECTION.

RAY and GANGULY (p. 907) have established a normal in the urinary constituents of Bengalee subjects. Compared with Americans and Europeans, this shows that the average diet is poor in protein. They followed up this work by investigations in epidemic dropsy, in which

the urine shows increased uric acid, reduced chlorides and reduced inorganic phosphorus, the latter constituting a good diagnostic sign.

LAL (p. 907) describes an outbreak of epidemic dropsy confined to a group of servants who messed together. Others in the household were not affected, though in close personal contact. All available evidence incriminates mustard oil, but the toxic component is not known. From careful work, LAL, AHMAD and ROY (p. 908) conclude that allylisothiocyanate, present in mustard oil, is not responsible for the symptoms of epidemic dropsy.

LAL and ROY (p. 909) give details of 8 outbreaks. They tested mustard oil used in 3 of these, using sound oil as control and volunteers using two of these oils, but not the third, developed epidemic dropsy. This evidence tends to confirm the mustard oil theory, but CHOPRA *et al.* (p. 909) produce evidence that symptoms indistinguishable from those of epidemic dropsy can be produced in man by the consumption of mustard oil to which has been added oil from the seeds of *Argemone mexicana*, but not by mustard oil alone. The toxic principle is destroyed by heating to 240°C., and the argemone seeds bear some resemblance to those of the mustard plant. LAL *et al.* (p. 910) have elaborated two chemical and two physical tests which indicate disease-producing mustard oil. The seeds of *Argemone mexicana* impart the physical and chemical properties of toxic oil to mustard oil and from argemone oil and toxic oil, but not from pure mustard oil, a white crystalline substance has been isolated which responds to the differential tests. This will be tested for toxicity.

SINHA (p. 911) describes the symptoms of an anomalous type of epidemic dropsy in which an acute cardiac crisis, without dropsy, occurs. Cyanosis and dyspnoea occur and the prognosis is bad. Treatment is unsatisfactory.

In nutritional oedema, SHUKRY *et al.* (p. 912) found hypochromic anaemia, hypoproteinaemia, reduced blood cholesterol and rise in chloride content of the oedema fluid—conditions found in animal experimental starvation oedema.

Vitamin deficiency, particularly vitamin C, is regarded by TROLLI (p. 912) as the principal cause of a syndrome seen in African children characterized by severe anaemia, loss of pigment especially in the hair, oedema and bleeding from the gums. Ankylostomiasis is often present and must be treated, but the essence of treatment is a generous diet. VAN DAELE (p. 913) in the Congo describes the condition Buaki which resembles this syndrome in many respects, though in Buaki there is no stomatitis. It responds to the administration of a well balanced mixed diet, and is thought to be due to excess of carbohydrate and lack of protein and vitamins. POUHIN (p. 913) describes a syndrome of oedema, sometimes with nervous symptoms, in Morocco. The diet of the inhabitants is low in animal protein, and the most successful treatment is the addition of meat and lemons.

VIDAL (p. 914) describes a mixed avitaminosis in children showing oedema of the legs, cyanosis, inflammation of the lips and gums and erythema. Gastro-intestinal disturbance is common. The condition resembles pellagra in some respects, and other deficiency diseases of children. Ankylostomiasis is not a factor.

DEBDAS (p. 914) records children who after long periods of diarrhoea developed purpuric symptoms and calls attention to the necessity of administering orange juice to ensure a sufficient supply when diet is restricted and elimination, in frequent stools, is rapid. *C. W.*

RAY (S. N.) & GANGULY (R.). **Urinary Composition of Normal Bengalee Subjects.**—*Indian Jl. Med. Res.* 1938. Oct. Vol. 26. No. 2. pp. 459–463. [13 refs.]

With a view to accounting for urinary conditions and constituents in disease it is important to have a standard which may be regarded as "normal" for comparison. The authors have tried to establish this in Bengalees by analyses of 24-hour specimens from middle class Hindu Bengalees, male and female, between the ages of 16 and 28, giving a history of good health during the preceding two years. In the original paper a table is given comparing the findings with those in Americans and Europeans. The two latter show closely approximating results, one to the other, but in certain particulars differ markedly from the Bengalee analyses. Thus urea excretion in the Bengalees was only 4·3 gm. in 24 hours (average of about 50 persons) as compared with 31·5 and 30 in Americans and Europeans respectively, and total nitrogen 4·83 as compared with 16·8 and 16·0; inorganic sulphates were 0·65 gm. as compared with 3·27 and 2·92 gm. Calcium excretion was also low 0·06 as compared with 0·17 and 0·15 respectively. It is curious to note that the excretion of uric acid 0·7 gm. is equal to that of the European and higher than that of the American, 0·64, while chloride excretion (17·4) is higher than in Americans (10–15 gm.). Neutral sulphates were the same 0·18, 0·18 and 0·17 respectively and ethereal sulphates 0·1, 0·19 and 0·22. These figures indicate that the average Bengalee diet is poor in food proteid, about 35 gm. of protein only per day, well below Chittenden's minimum. *H. H. S.*

RAY (S. N.) & GANGULY (R.). **Observations on the Metabolic Activity of Patients suffering from Epidemic Dropsy. Part I. Urinary Composition of Epidemic-Dropsy Patients.**—*Indian Jl. Med. Res.* 1938. Oct. Vol. 26. No. 2. pp. 465–468.

Following up their analyses of normal urinary constituents in Bengalees (see above) the authors have turned their attention to pathological conditions and deal first with epidemic dropsy. The chief alterations, as shown in a table, were: an increase of uric acid excreted, 0·94 as compared with the normal 0·7 gm., a reduction by about one-third in chloride (11·4 as compared with 17·4) and a reduction of inorganic phosphorus to one-sixth, 0·11 as compared with normal 0·68. The ethereal sulphate was not altered, a fact which militates against the idea that the cause is an intestinal bacterium or bacterial toxin, at all events of a phenolic nature.

The increase of uric acid in epidemic dropsy had been previously noted and is ascribed to disturbance of the cell nuclei. The low excretion of inorganic phosphates may be utilized, in the authors' view, as a sign of diagnostic value in suspected cases. The lowered output of chlorides is due to retention, for the diet was the same; this is corroborated by finding increased concentration of chlorides in the blood during an attack of epidemic dropsy. *H. H. S.*

LAL (R. B.). **Further Studies in Epidemic Dropsy.**—*Calcutta Med. Jl.* 1938. Sept. Vol. 34. No. 3. pp. 169–182. With 2 plans & 3 figs. on 2 plates.

CALCUTTA MEDICAL JOURNAL. 1938. Sept. Vol. 34. No. 3. pp. 218–221.—**The Epidemic Dropsy Problem.**

Dr. Lal, who is probably the best authority on this condition at the present day, having done much experimental work and epidemiological

studies on epidemic dropsy, here recounts further work of a like nature. He reviews briefly the outbreaks at Kharagpur, Rangpur, and Kidderpore, and tabulates the main findings of BHARGAVA at Benares, Allahabad and Cawnpore, and at the last named those of BANNERJEE also. The Khargpur outbreak in July and August 1937 involved 124 cases in 38 families; that at Rangpur 65 in 24 families in three different areas; that at Kidderpore was a small outbreak occurring in a merchant's household and confined to a group of servants who messed together, whereas others living in a close association but with different kitchens escaped; thus intimate personal contact was present without transference or spread of the disease.

All the available evidence still tends to support the theory that mustard oil is the cause, but which constituent or what adulterant of it is as yet undetermined. Experiment so far disproves allylisothiocyanate which is responsible for the pungency of the oil. One of the main difficulties lies in the fact that the disease has not, up to the present, been reproduced in animals. The pathological changes in the skin are well represented by photomicrographs in the article.

The editorial gives a general review of the question and discusses briefly the theories held as regards the aetiology of the condition, namely avitaminosis, rice, infection, and toxin (mustard oil or some abnormal constituent of it). *H. H. S.*

LAL (R. B.), AHMAD (Bashir) & ROY (S. C.). **Investigations into the Epidemiology of Epidemic Dropsy. Part VI. Allylisothiocyanate as an Aetiological Factor in Epidemic Dropsy.**—*Indian Jl. Med. Res.* 1938. July. Vol. 26. No. 1. pp. 213–228.

All the positive evidence we have goes to show that certain consignments of mustard oil have been associated, apparently aetiologically with the symptoms of epidemic dropsy among those who have consumed it. The next step in the investigation is to determine whether the symptoms are due to some constituent of the oil itself or to some adulterant (*cf.* triorthocresolphosphate as an adulterant of Jamaica ginger causing "Jake paralysis," see *Bull. of Hyg.*, 1931, Vol. 6, pp. 99, 207, 248, 443, 717 and 1932, Vol. 7, pp. 389, 585). This is not easy in the case of mustard oil because the Bengalis (who suffer most) buy it as a rule in small quantities at a time and the investigator is not able to obtain quantities sufficient for his experiments. Further, up to the present, it has not been possible to reproduce the symptoms of epidemic dropsy in laboratory animals.

In this article the authors recount their study of allylisothiocyanate a constituent of the oil and liberated from a glucoside, sinigrin, by the action of a ferment, myrosin, both present in the oil. Allylisothiocyanate is a powerful irritant and if in excess might be expected to cause gastro-intestinal disturbance which is an early symptom of epidemic dropsy.

The authors describe the method of estimating the allylisothiocyanate (a point of particular interest to chemists) and the effect of feeding experiments on rats, adult and young, and cats and monkeys. Details of the many tests are given, described in letterpress and presented also in protocols. In no case were the symptoms of epidemic dropsy produced, and human subjects were able to take food cooked in oil containing as much as 2,517 mgm. of allylisothiocyanate for 30 days without ill effects. Also nearly nine-tenths of this substance

is lost during the process of cooking. The conclusion is that the deleterious substance in the mustard oil is not allylisothiocyanate. This evidence based on careful research, though negative, is of the utmost importance. *H. H. S.*

LAL (R. B.) & ROY (S. C.). **Investigations into the Epidemiology of Epidemic Dropsy. Part VII. Further Field Studies and Controlled Experiments.**—*Indian Jl. Med. Res.* 1939. July. Vol. 27. No. 1. pp. 191–206. With 3 diagrams.

The author gives notes of eight outbreaks of epidemic dropsy, with diagrams illustrating the distribution of cases in three of them. The following table, compiled from the information in the text, gives the main points of the outbreaks :—

Place	Date	Cases	Families
Khargpur	15–24th August, 1937	124	38
Garpar	24–28th August, 1937	52	12
Kidderpore	8–11th January, 1938	6	1*
Rangpur	16–19th January, 1938	65	24
Alamdangar	21–25th January, 1938	32	15
Calcutta Medical School	9–14th June, 1938	13(?18)	1 group†
Manirampur	27th June–4th July, 1938	98	22
Suri	9–11th July, 1938	20	9

* The Kidderpore outbreak was a small one involving the household of a merchant ; there were 14 members comprising, as regards messing, (1) the householder, his wife and 3 children ; (2) three male and three female servants ; (3) two shop assistants and a motor-car driver. Only group 2 suffered, but all of them ; they used Bengalee diet and mustard oil exclusively for cooking-fat. Gastro-intestinal symptoms developed after a week, during which each had consumed about 8 oz. of the oil, and oedema was present in another week or ten days.

† The Calcutta Medical School residents comprised, as regards messing, four groups : (a) Patients, 155 in number ; (b) Pathologist, nurses, cooks and compounders (32 in all) ; (c) House surgeons (9), and (d) the Resident Medical Officer. Among these, 9 nurses, 2 cooks (4 other cooks doubtful), the pathologist and one, possibly two, compounders were affected. Altogether 13 certain cases and 5 others doubtful, and all in group (b) which used the largest amount of mustard oil.

The authors collected samples of the mustard oil definitely associated with three of these outbreaks and tested their toxicity on volunteers, with gaol-produced sound oil as a control. With the oils from Alamdanga and Rangpur cases developed, but not with the Khargpur samples ; only three volunteers were fed with each. This evidence tends to confirm the mustard oil theory of the cause of epidemic dropsy.

H. H. S.

CHOPRA (R. N.), PASRICHA (C. L.), GOYAL (R. K.), LAL (S.) & SEN (A. K.). **The Experimental Production of Syndrome of Epidemic Dropsy in Man.**—*Indian Med. Gaz.* 1939. Apr. Vol. 74. No. 4. pp. 193–195.

The "mustard oil theory" of epidemic dropsy is not new, but experimental study of the actual cause has long been wanting, hence the value of this important paper. SARKAR in 1926 recorded symptoms

resembling those of epidemic dropsy following consumption of mustard oil adulterated with *sialkata* or *katakar* oil, argemone oil [see this *Bulletin*, 1927, Vol. 24, p. 238] and two years later KAMATH reported the Ganjam outbreak where *odissimari* seeds were implicated [this *Bulletin*, 1929, Vol. 26, p. 355]. More recently the work of LAL, ROY and GHOSAL has thrown fresh light on the question [this *Bulletin*, 1938, Vol. 35, p. 312].

In oils obtained from houses where there had been cases of epidemic dropsy positive reactions for argemone oil were obtained, and odissimari seeds were shown to be seeds of *Argemone mexicana*.

Volunteers were divided into three groups: For one the food was cooked in pure mustard oil to which known quantities of argemone oil were added; for the second the food was cooked in samples of oil giving argemone oil reactions and implicated in natural outbreaks of the disease; the third group had a similar diet but the food was cooked in mustard oil giving no reaction for argemone oil. The results of the experiments are given in two protocols. Some of the symptoms of the disease appeared in those receiving argemone oil, which seems to have a cumulative effect; provided a certain quantity is taken the symptoms appear after an interval, though consumption of the oil is stopped. Its toxic principle is destroyed by heating to 240°C., not at 150°C.

The authors conclude that ingestion of the oil expressed from the seeds of *Argemone mexicana* can produce the symptoms of epidemic dropsy, but

"Whether the condition produced is identical or not with the naturally-occurring epidemic dropsy cannot be definitely said at present, but there is no doubt that the use of oil containing argemone oil is harmful to man. There appears to be little doubt that consumption of adulterated oil produces symptoms which cannot be distinguished from those encountered in the naturally-occurring disease.

"From the evidence available it appears that the adulteration of mustard oil with argemone oil may or may not be intentional on the part of those who grow the mustard plant, or of those who express or sell the oil. The plant *Argemone mexicana* is widespread, its seeds bear a superficial resemblance to mustard seeds and may be harvested along with them. It is possible that, because oil can be obtained from the seeds of this plant, efforts are not made to exclude these seeds in the harvesting of mustard seeds." *H. H. S.*

LAL (R. B.), MUKHERJI (S. P.), ROY (S. C.) & SANKARAN (G.). **Investigations into the Epidemiology of Epidemic Dropsy. Part VIII. Studies on the Nature and Origin of Certain (? Toxic) Substances Present in the Supplies of Mustard Oil associated with Outbreaks of Epidemic Dropsy.**—*Indian Jl. Med. Res.* 1939. July. Vol. 27. No. 1. pp. 207–224. With 7 figs. on 2 plates.

In pursuance of their work on epidemic dropsy the authors, on the assumption that the cause is to be found connected with the mustard oil used, carried out investigations to determine the offending constituent. Their first step was to discover some tests which would distinguish sound from disease-producing oil. They found two chemical and two physical tests. The chemical are: (1) The Nitric Acid test. When a little of the oil is vigorously shaken with an equal quantity of concentrated HNO_3, in the case of toxic oil a brownish red colour develops in the bottom acid layer. (2) The Cupric Acetate

test. If a mixture of the oil acidified with glacial acetic acid and 3 per cent. solution of cupric acetate be heated in a water-bath for 15 minutes, in the case of a toxic oil a precipitate forms and the colour of the watery layer changes from blue to green. The physical tests are: (1) Spectroscopic. Whereas the general nature of the spectrum is the same in toxic and non-toxic, the latter show a broad absorption band between 2,900 and 2,600 A.U. with maxima near 2,750. (2) Fluorescence on exposure to ultra-violet rays, absent in sound oils.

Results of these tests are given in the subjoined table:—

Test		Epidemiological history and toxicity positive (class I)	Epidemiological history and toxicity negative (class II)
Nitric acid test	Positive ...	21	2
	Negative ...	2	21
Cupric acetate test	Positive ...	21	0
	Negative ...	2	23
Fluorescence test	Positive ...	22	11
	Negative ...	1	12

The authors next set out to determine whether the poisonous effects were due to deteriorated mustard seeds, to adulteration of the oil, or adulteration of the seeds. They found that seeds of *Argemone mexicana*, which resemble the black mustard seed *Brassica napus*, impart the physical and chemical properties of toxic oil to mustard oil, and either accidentally or by deliberate adulteration these find their way into stocks of mustard seed and the expressed oil is present in sufficient amount in the final product to cause the symptoms observed in the outbreaks of epidemic dropsy. Further, from oil of *Argemone mexicana* and from a proved toxic oil (but not from pure mustard oil) a white crystalline substance has been isolated which responds to the differential tests. Study is to be undertaken to determine whether this is the actual toxic substance. *H. H. S.*

SINHA (B. C.). **Some Special Clinical Aspect of Epidemic Dropsy and the Limitations of its Treatment.**—*Trans. Med. College Re-Union.* Calcutta. 1938–39. Vol. 2. pp. 81–84.

The author has lately had under observation patients suffering from epidemic dropsy of an anomalous type, in short "epidemic dropsy without dropsy," but with acute cardiac crisis. The first observed symptom is usually intense dyspnoea of sudden onset, but enquiry reveals cases of epidemic dropsy in other members of the family. Cyanosis is present, but not very marked. All show some degree of cardiac enlargement, with more or less tumultuous action but without irregularity; the pulmonary second sound is accentuated and there may be a soft systolic murmur at the apex. Pulse is 100–140, regular, of low tension; blood pressure 100–130 mm. systolic, 50–70 diastolic. The liver is enlarged and tender. The prognosis is grave; four patients referred to in this article all died within 3–4 days.

The cause of the dyspnoea is discussed, whether central or due to impending ventricular failure. Treatment is very unsatisfactory and disappointing. Patients gain some ease by being propped up in bed and by injections twice daily of 1 cc. luminal and 1/100 grain of atropin. Venesection and abstraction of 8–10 oz. daily for 2–3 days may relieve, but not after the first few days; inhalation of oxygen gave no relief; ephedrine and adrenaline were without effect, digitalis and stropanthine made no impression when there was tachycardia; glucose proved useless. Sleeplessness was a troublesome symptom which was unrelieved by the usual hypnotics. *H. H. S.*

SHUKRY (H.), MAHDI (M. A.) & EL GHOLMY (A. A.). **Nutritional Oedema in Children in Egypt.**—*Arch. Dis. in Childhood.* 1938. Sept. Vol. 13. No. 75. pp. 254–257. [Summary appears also in *Bulletin of Hygiene.*]

The authors have investigated eighteen cases in Egypt, children ranging in age between 1½ and 10 years, suffering from gastro-intestinal disorder with oedema. Theoretically, oedema develops when (1) the colloid osmotic pressure of the plasma becomes less than that of the cellular fluid; (2) there is increased permeability of capillary endothelium to salt and water; and (3) abnormal mechanical forces are acting.

In all but three the total serum protein was 4·5 per cent. or less, *i.e.*, the "critical level" of experimental oedema. The chlorides showed an increase of 120 mgm. per cent. or more, in one case 482 mgm., difference between the blood and oedema fluids, instead of the usual 50 mgm. per cent. higher in the cellular spaces. A table of detailed findings demonstrates an almost constantly present hypoproteinaemia, and the increased chloride content of the oedema fluid. By experiments on dogs the authors concluded that the return of serum protein to normal level is probably determined not only by adequate diet but also by the time needed for restoration of the activity of the liver and other tissues concerned with protein synthesis. Enlargement of liver with marked pallor and cellular changes were observed after death in some of the cases.

All the eighteen patients had definite hypochromic anaemia, hypoproteinaemia, reduced blood cholesterol and rise in chloride content of the oedema fluid—conditions found in animal experimental starvation oedema. *H. H. S.*

TROLLI (G.). Syndrome oedémateux, cutané et dyschromique. Note préliminaire d'après les médecins du Foréami. [**Oedema and Depigmentation of the Skin and Cutaneous Structures.**]—pp. 37–57. With 1 fig. 1938. Brussels: Fonds Reine Elisabeth pour l'Assistance Médicale aux Indigènes du Congo Belge, 112 rue du Commerce.

The syndrome described in this article goes by the local names of Mbwagi, Kikuba, and Kibengi (from benga=to grow white), or, by the French doctors, "cheveux blancs." The established disease is characterized by oedema of the integument causing a waxy appearance, by severe anaemia, loss of pigment in the hair, weakness, articular pains, bleeding from the gums and, in some cases, enlargement of the spleen. Children are mostly attacked; of 1,450 cases 1,095 (75·5 per

cent.) were children, 211 were adult female and 44 men ; many of the children were still being breast-fed.

The following is a more detailed account of the symptoms and course of the disease : the onset is gradual with loss of appetite ; this is followed by marked weakness, pallor of skin and hair, the skin becoming lemon-yellow, dry and scaly ; haemic murmurs develop with foetal cardiac rhythm, the liver enlarges, red cells 3,000,000 or so, haemoglobin 60–70 per cent., white cells 6,000–8,000, with relative lymphocytosis and an Arneth index deviated to the right, no marked eosinophilia ; recession of the gums with alveolar periostitis ; in the later stages cardiac signs increase, the abdomen enlarges and the face is swollen and puffy and the hair becomes less and less pigmented. The fatality rate is in the neighbourhood of 15 per cent. Some are infested with hookworms, but the general opinion is that the cause is a vitamin deficiency, in particular vitamin C. Treatment is mainly based on these lines—clearing up the ankylostomiasis if present, giving a generous diet, rich in vitamins, and cardiac and general tonics. *H. H. S.*

VAN DAELE (G.). Sur une affection de carence et de déséquilibre diététique observée au Congo (Buaki des indigènes). [**Buaki, a Deficiency Disease in the Congo.**]—*Ann. Soc. Belge de Méd. Trop.* 1938. Dec. 31. Vol. 18. No. 4. pp. 653–669.

Among the inhabitants of many villages in certain parts of Kwango (Congo) some proportion may be immediately picked out as suffering from an affection giving rise to a very characteristic appearance : a dull, dry, rough, scaly or nutmeg-grater-like skin with general loss of pigment of varying degree ; desquamation of the skin of the palms and soles ; the hair thinned, lank and depigmented with perhaps patches of alopecia ; loss of weight and muscular wasting, sometimes cachexia ; the face puffy, the lower extremities oedematous as also the genitalia ; a distended abdomen with moderate ascites and sometimes mild diarrhoea ; periarticular rheumatic pains and marked anaemia complete the picture. On the other hand there are no signs referable to the nervous system or special senses, no visceral or bony lesions, no other gastro-intestinal symptoms, no stomatitis, no albuminuria. The affection is recognized by the natives and called Buaki. It affects women and children, chiefly the forsaken wife or the orphan, very rarely a male ; this incidence at once suggesting that it is a condition due to dietetic deficiency. The diet at best consists of manioc with a minimum of maize and ground nuts, rarely bananas, beans and fruits are hardly known, meat is never eaten and the only supplements may be insects, small animals, roots and a little palm wine. The condition does not respond to an exhibition of vitamins but improves when a well balanced mixed diet is given. It is therefore considered to be due to an unequilibrated diet in which there is an excess of carbohydrate but lack of protein, probably in association with vitamin insufficiency.

H. S. S.

POUHIN (E.). Syndromes d'oedèmes par carence alimentaire dans le cercle de Zagora (Maroc). [**Oedema from Diet Deficiency in Zagora (Morocco).**]—*Bull. Soc. Path. Exot.* 1939. July 12. Vol. 32. No. 7. pp. 769–779.

The author during a residence of 2¼ years in the district saw several cases of oedema due to more than one cause. Some seemed to be

malarial in origin and cleared up when quinine was given ; others were due to insufficient food—a famine oedema, others again to debility following typhus, and a fourth class ascribed to imbalance of diet. Only four showed any nervous symptoms, two with polyneuritis of the legs and flaccid paraplegia and two with polyneuritis of one side affecting mainly the extensors. All four recovered, two of them promptly on being given vitamin B_1.

Analysis of the diet of the inhabitants of Draa shows a definite reduction of animal proteins below the amount necessary for adequate nutrition and as for vitamin content—dates were the main source—100 gm. yielded 200 units of vitamin A, 30 I.U. of B_1, traces only of B_2 and no C or D (sometimes traces of the last). Administration of synthetic vitamin had little effect, the most successful treatment was addition of meat and lemons. *H. H. S.*

VIDAL (Antonio). Avitaminosis compleja infantil. [**Mixed Avitaminoses in Children.**]—V Congreso Médico de Centro América y Panamá. 6 pp. With 5 figs.

The chief symptoms of the condition described [as occurring in Honduras ?] are : oedema of the legs, and involving sometimes the arms and face, coldness of the extremities, with cyanosis, congestion, perhaps inflammation of lips and gums—signo del colorete (the rouge sign)—and in some a certain degree of stomatitis. An erythema of the legs may extend over the abdomen and nates and even to the arms. It resembles pellagra in being symmetrical and in severe cases desquamation may continue for weeks or even months. As in pellagra too there occur attacks of gastro-intestinal disturbance with diarrhoea in nearly all cases. Bleeding from the gums is sometimes seen, and conjunctivitis and xerosis. The blood shows little change beyond a moderate anaemia and reduction of haemoglobin. The oedema is not due to ankylostomiasis. Those affected are of the poorer classes, living in insanitary conditions, on a diet consisting largely of maize. There is considerable resemblance to the " culebrilla " of Mexico [see this *Bulletin*, 1937, Vol. 34, p. 247 and *Bull. of Hyg.*, 1935, Vol. 10, p. 806] and kwashiorkor of the Gold Coast [see this *Bulletin*, 1934, Vol. 31, p. 344 and *Bull. of Hyg.*, 1936, Vol. 11, p. 311].

The present article records 15 patients, of ages ranging between 15 months and 6 years, but it is said to be most common between two and four years. Sex seems to play no part ; of these 15, eight were boys and seven were girls ; five died, three males and two females. If coming under observation in time, they did best on a generous diet of milk, eggs, green food, tomato-juice, and for medicine calcium lactate. *H. H. S.*

DEBDAS (Nanigopal). **Secondary Purpura in Chronic Diarrhoea in Children due to Hypovitaminosis-C.**—*Calcutta Med. Jl.* 1939. May. Vol. 35. No. 5. pp. 384–386.

Three cases are recorded of children who after troublesome diarrhoea over periods of 6 to 12 weeks developed purpuric symptoms. The author ascribes this secondary purpura to two causes : first, that on account of the diarrhoea the diet was restricted and vitamin C deficient, and, second, that what was ingested was rapidly got rid of in the frequent motions. It is important, therefore, in such cases not to keep

too much or too long to starchy foods and to give vitamin C as orange-juice; the amount needed of the latter is not sufficient to aggravate the diarrhoea. *H. H. S.*

SEQUEIRA (James H.). Cutaneous Manifestations of Vitamin Deficiency. —*East African Med. Jl.* 1938. July. Vol. 15. No. 4. pp. 96–110. With 4 figs. on 2 plates. [28 refs.] Discussion pp. 110–115.

MALARIA.

PRÉCIS OF ABSTRACTS IN THIS SECTION.

COVELL (p. 917) has given a full account of the history of malaria in Delhi.

Two persons reported by TANGUY (p. 917) contracted malaria near Fréjus in the French Riviera.

HÉRIVAUX *et al.* (p. 918) have studied malaria in the New Hebrides. The form is mild but *P. falciparum* is the most common parasite. There is a marked relationship between malaria and rainfall, suggesting seasonal breeding of *A. punctulatus*, the only Anopheles found, which is found to have very catholic habits. Eradication of this mosquito might be comparatively easy.

MISSIROLI (p. 919) discusses the nomenclature of *P. falciparum* and GIOVANNOLA (p. 919) concludes that *P. tenue* is not a valid species.

ROUBAUD (p. 919) shows that exceptional individuals of *A. maculipennis labranchiae*, usually markedly anthropophilic, may show zoophilic tendencies. In Portugal, CAMBOURNAC (p. 920) found larvae of *A. maculipennis atroparvus* generally spread throughout ricefields, but more numerous when there was growth of the alga Spirogyra. There is considerable mortality in each larval instar. WEYER and BOCK (p. 920) found a higher mortality in infected than in non-infected mosquitoes. *A. maculipennis* transmits *P. vivax* better than *P. falciparum*, the latter being best transmitted by *A. superpictus* among the Anopheles used and giving an infective index of 81 per cent. POTTER and HOCKING (p. 921) have devised an apparatus for testing the effect of insecticides on flying insects, and from which samples of air can be removed for examination.

BOYD *et al.* (p. 922) showed experimentally in man that current or recent infection with either *P. vivax* or *P. falciparum* in no way interferes with successful infection with the other.

The injection of non-specific protein (*e.g.*, milk) is considered by SCHLESINGER (p. 922) to cause the coarsening of granulations existing in the blood cells, thus rendering them visible. In a proportion of patients with latent malaria this procedure caused typical Schüffner's or Maurer's dots to appear.

LENTJES (p. 923) reports that in fresh benign tertian infections 0·6 gm. hydrochloride of hydroquinine daily for 7 days is superior to quinine. It cuts short the attack promptly, inhibits the production of gametes, diminishes relapses and has little toxicity. HAUER (p. 923) quotes a patient in whose family hypersensitivity to quinine, in the form of general urticaria, has been present through three generations.

CIUCA *et al.* (p. 924) show that quinine and atebrin, even if combined with plasmoquine, do not prevent the appearance of gametocytes,

but a single dose of 2 cgm. plasmoquine will eliminate existing gametocytes as effectively as large daily doses. It is therefore logical to give this dose 3 or 4 days after completion of a course of schizonticidal drugs, and to repeat it at intervals of 5 days.

During atebrin treatment BOCK (p. 924) has noted clumping followed by extrusion of the pigment, solution of the cytoplasm and shrinking and breaking up of the chromatin. The effect is therefore apparently directly on the parasites. KOSTIĆ and ANTIĆ (p. 924) gave 0·4 gm. atebrin each week to a carefully observed group of prisoners and warders in Jugoslavia. This dose was divided between two successive days. The infection rate diminished, there were no ill-effects and all continued at work, whereas in the controls the infection rate increased considerably.

SINTON *et al.* (p. 925) come to the conclusion that proseptasine appears to have a true causal prophylactic action against the sporozoites, or forms between sporozoite and trophozoite, of the strain of *P. falciparum* used in careful experiments on 8 patients.

MACDONALD (p. 926) has designed a cheap, effective syphon for the automatic flushing of streams in the control of *A. culicifacies* breeding in Ceylon. In Freetown the investigations of PEASTON and RENNER (p. 926) indicate that an area hyperendemic in 1926 has been converted to a condition of endemicity like that of the rest of the town, probably owing to the permanent canalization of a watercourse and drainage into it.

Malaria of monkeys and birds.—Using an antigen prepared from the parasitized red cells of monkeys dying from *P. knowlesi* infection, EATON and COGGESHALL (p. 926) observed strong complement fixation with sera of persons infected with *P. knowlesi*, *P. vivax* or *P. falciparum*. The reaction is therefore group specific. MOSNA (p. 927) shows that immune bodies are developed in the serum of monkeys with *P. knowlesi* infection, which, when injected in large quantities into others at the time of infection, modify the disease to a chronic, rather than immediately fatal, infection.

RODHAIN *et al.* (p. 928) failed to infect man and other monkeys with the parasite of chimpanzees which resembles *P. vivax*. They therefore consider it to be a distinct species. BRUMPT (p. 928) considers that the three plasmodia of chimpanzees which resemble the three common parasites of man, are probably, on morphological and pathogenic grounds, distinct from the latter. One is known as *P. reichenowi* and he suggests that the others be named *P. schwetzi* and *P. rodhaini*.

ROUBAUD *et al.* (p. 928) find that *Aëdes geniculatus* permits complete development of *P. gallinaceum*.

HENRY (p. 929) shows that the blood of fowls infected with *P. gallinaceum* by means of mosquitoes is not itself infective for 4 or 5 days.

HEWITT (p. 929) confirms the finding that young *P. cathemerium* parasites enter young red cells only, both reaching maturity at about the same time, except during the crises, when exceptionally young red cells are present and are attacked.

GAVRILOV *et al.* (p. 929) found that *P. gallinaceum* survived for 10 days in culture of bone marrow, but failed to do so in fowl spleen tissue culture.

HEGNER and WOLFSON (p. 929) failed to separate erythrocytic and exoerythrocytic schizonts by means of tissue culture of infected brain, lungs and spleen, and inoculation into birds.

GIOVANNOLA (p. 930) considers the toxoplasma-like bodies seen in *P. gallinaceum* infections of fowls to be stages in the development of that parasite, and calls attention to two inclusions, probably parasitic, in the mononuclear blood cells. CHORTIS (p. 930) considers that exoerythrocytic schizonts are forms which develop abnormally after ingestion of young parasites by the reticulo-endothelial cells, the latter showing some loss of function. The reticulo-endothelial system shows marked proliferation in *P. gallinaceum* infections. RAFFAELE (p. 931) suggests that the exoerythrocytic schizonts of birds may give rise to two kinds of merozoites, one for continuance of exoerythrocytic development, the other for initiation of erythrocytic development. A similar cycle may occur in man.

Only the exoerythrocytic schizonts in *P. gallinaceum* infection give a definite reaction by Feulgen's method, according to UNGO-MUGDAN (p. 931).

Mosquito transmission was responsible for an outbreak of *P. relictum* infection in penguins in Antwerp, and RODHAIN (p. 931) found exoerythrocytic schizonts in these birds and in another infected by inoculation. These schizonts are more resistant to atebrin than the ordinary parasites.

DÉMINA (p. 932) studied the natural resistance of birds to *P. relictum.*

MOSHKOVSKY and SYRKINE (p. 932) found that certain acridine compounds, active against bird malaria, cause the appearance of small granules in the red cells of mice and birds.

DURAND and VILLAIN (p. 932) failed to influence infection in pigeons with *Haemoproteus columbae* by the use of sulphanilamide derivatives.

C. W.

COVELL (G.). **Antimalaria Operations in Delhi. Part I.**—*Jl. Malaria Inst. of India.* 1939. Mar. Vol. 2. No. 1. pp. 1–61. With 6 maps (1 folding), 1 chart & 26 figs. on 13 plates. [20 refs.]

This part of the report contains a detailed account of the history of malaria in Delhi, of the nature of the malaria problems in different parts of the Delhi urban area, and of the distribution and intensity of malaria infection in Delhi in 1936 when the last antimalaria campaign was started. Clear maps, good photographs of different types of anopheline breeding places, abundant tables giving weekly climatic data for seven years, morbidity data, mortality data, and spleen rates recorded by different observers between 1909 and 1936 supplement the letterpress. It is an unusually fully documented report and in consequence does not lend itself to summary in small space.

Norman White.

TANGUY (Y.). Observation de paludisme contracté en France (Saint-Aygulf). [**Malaria contracted in France.**]—*Bull. Soc. Path. Exot.* 1939. Mar. 8. Vol. 32. No. 3. pp. 285–286.

This is a brief note concerning a patient who acquired a *P. vivax* infection in the south of France. She had never been outside France and never visited any place where malaria is endemic. During three years she passed some of the summer months in Saint-Aygulf, in a house one and a-half kilometres distant from the military camp at

Fréjus in the Riviera. During the last of these visits in 1937 she contracted malaria. Her husband appears to have contracted the disease at the same time. *N. W.*

HÉRIVAUX (A.), RONCIN (P.) & DAO VAN THAI. Contribution à l'étude du paludisme des Nouvelles-Hébrides. Recherches effectuées à Port-Vila et alentours. [**Malaria in the New Hebrides. Investigations in Port Vila and Neighbourhood.**]—*Ann. de Méd. et de Pharm. Colon.* 1939. Jan.–Feb.–Mar. Vol. 37. No. 1. pp. 40–62. With 6 graphs.

This report is of special interest because, apart from BUXTON's Report [this *Bulletin*, 1927, Vol. 24, p. 941] on the Islands of the Southern Pacific, no precise information has been published about malaria in the New Hebrides. From the malaria point of view the New Hebrides are of special interest because they mark the limit of extension of indigenous malaria in the Pacific to the south and east. In Fiji and New Caledonia, relatively so near to the New Hebrides, as distances go in the Pacific, indigenous malaria is unknown.

The year's observations recorded were carried out in and around Port Vila in the Island of Vaté, the chief island of the group. Vaté has 2,800 inhabitants half of whom live in Port Vila. There are 1,600 belonging to the indigenous Melanesian race, 500 Europeans, French and English, and 700 Asiatics. Not all are of pure descent. There are numerous half-castes especially among the French population. The authors refer to the mixture of blood as a " cocktail of blood " !

In the French Hospital at Port Vila, of 3,102 patients treated during 1937 (both in-patients and out-patients) 604 were suffering from malaria. The disease occurs in mild form and is hardly ever fatal, even among infants. It is very amenable to treatment. Pernicious attacks are very rare ; there were two in 1937, both among natives. Haemoglobinuric cases occur from time to time, chiefly among Asiatics, but even these cases are rarely fatal.

Parasites were found in 307 cases during the year. *P. falciparum* was found in 242, *vivax* in 61, both in 4. *P. malariae* was never seen. Of 129 school-children aged 5 to 12 examined, 47 had palpable spleens, a spleen rate of 36·4 (not 42·7 as printed in error). The spleen index of 156 members of the labour-force community, of Tonking origin, in the neighbourhood of Port Vila was 69·23 per cent.

The study of indigenous malaria is complicated by the arrival three or four times a year of batches of labourers from Tonking, for work on the French plantations. After a short period of observation at Port Vila these workers are distributed throughout the islands, a considerable number each time remaining in Vaté. Numerous attacks of acute malaria are commonly observed among them for a month or two after their arrival unless they happen to arrive in the cool season.

Indigenous malaria of local origin is almost non-existent during the three cool months, July to September, rises with the advent of the hot weather and is at its worst towards the close of the hot season, when daily variations in temperature are most marked, generally in the month of May. There appears to be a marked relationship between the incidence of malaria and rainfall, a fact which would indicate that the most important anopheline breeding places are temporary and seasonal. This conclusion was confirmed by the observations made.

The only Anopheline was identified by Buxton 14 years ago, *A. punctulatus*. No other has been found. The author's observations indicate a marked catholicity in its breeding habits. Larvae have been found in shade and in full sunshine, in stagnant and in running water, in clear and in muddy waters, in large marshes and in small puddles, in small artificial collections of water, in fresh and in very saline water. It is a domestic mosquito profiting by household negligence. Adults do not appear to fly far. Its eradication might be neither difficult nor costly. *N. W.*

MISSIROLI (A.). *Plasmodium immaculatum*, Grassi e Feletti (1892), Schaudinn (1902), nome corretto del parassita della terzana maligna. [*P. immaculatum* **Correct Name of the Parasite of Malignant Tertian Malaria.**]—*Riv. di Parassit.* Rome. 1938. Dec. Vol. 2. No. 4. pp. 269–273. English summary (6 lines).

In this paper the author reviews the early papers of GRASSI and FELETTI dealing with the parasites of human and avian malaria. He concludes that the correct name for the parasite of avian malaria is *Plasmodium praecox* Grassi and Feletti, 1890, *P. relictum* being a synonym, while that of the human parasite is *Plasmodium immaculatum* Grassi and Feletti, 1892, with *P. falciparum* as a synonym [see also this *Bulletin*, 1939, Vol. 36, p. 390]. *C. M. Wenyon.*

GIOVANNOLA (Arnaldo). Ceppi tropicali e ceppi europei di *Plasmodium immaculatum*. [**Tropical and European Strains of** *P. immaculatum*.] —*Riv. di Parassit.* Rome. 1938. Dec. Vol. 2. No. 4. pp. 289–304. With 5 figs., 1 graph & 1 plate. [23 refs.] English summary.

Comparing a strain of malignant tertian malarial parasite of Ethiopian origin with one from the Roman Campagna during maintenance in general paralytics, the author has observed that in infections due to the tropical strain fully developed schizonts and young crescents occur commonly in the peripheral blood in cases which cannot be regarded as grave. Other features of the tropical parasites are a paucity of pigment, the presence of fair-sized rings in the blood and a marked susceptibility to quinine. Differences were also noted in the crescents, due largely to the appearance of the young crescents in the blood in the case of the tropical strain. It is concluded that *Plasmodium tenue* is not a valid species, while the tropical strain should be known as *Plasmodium immaculatum* var. *perniciosum* (Ziemann, 1915). [See MISSIROLI above.] *C. M. W.*

ROUBAUD (E.). Le comportement anthropophile de l'*Anopheles maculipennis labranchiae*, étudié dans les conditions expérimentales en insectarium. [**Anthropophilic Behaviour of** *A. maculipennis labranchiae* **under Experimental Conditions in Insectarium.**]—*Bull. Soc. Path. Exot.* 1939. Mar. 8. Vol. 32. No. 3. pp. 295–297.

Observations, hitherto unpublished, carried out six years ago on a strain of *A. maculipennis labranchiae* obtained from the south of Spain, showed the persistence with which this paucidentate species retains its anthropophilic feeding habits to the third generation bred in captivity. Experiments carried out in small cages, 1/20 cubic metre, revealed the fact, however, that in any given lot bred together certain individual

mosquitoes might display more or less constantly a more marked preference for the experimental animal, guineapig in this case, than for man. Exceptional individuals of a markedly anthropophilic species of mosquito may display zoophilic tendencies. *N. W.*

CAMBOURNAC (F. J. C.). **A Method for determining the Larval Anopheles Population and its Distribution in Rice Fields and Other Breeding Places.**—*Riv. di Malariologia.* Sez. I. 1939. Vol. 18. No. 1. pp. 17–22. With 3 figs.

The author of this interesting paper has collected quantitative information about the number of larvae and pupae of Anopheles present in a natural breeding place at different times of year. He makes use of a sampling method similar to the " quadrats " used by some botanists.

The investigation was made in rice fields in Portugal in which there were large numbers of early stages of *A. maculipennis atroparvus*. The author had a square bottomless box which could be set down at random in the shallow water of the rice field and which enclosed an area of 0·1 sq. m. Larvae and pupae enclosed in this area were then removed and counted. One sample was taken from each 2 sq. m. of a single rice plot and this was repeated monthly, in June, July and August. As it took 10 to 15 minutes to collect larvae and pupae (eggs were apparently neglected) from each sample, the method is laborious. The author found that the larvae were generally distributed through the rice plot and not more numerous at the edges. They tended to be more numerous wherever there was a growth of the alga Spirogyra and rarer in the presence of duckweed (Lemna). The total number of larvae per sq. m. fell from 400 in June to 62 in August. There was a considerable mortality which made itself apparent in each of the larval instars and which greatly reduced the output of adults. Indeed, in July and also in August, in 90 samples of 0·1 sq. m. each, the author found 1,300 larvae in the fourth instar, but no pupae at all.

The method is clearly capable of development in several directions and may lead to important results. *P. A. Buxton.*

WEYER (F.) & BOCK (E.). Versuche zur Uebertragung verschiedener Plasmodien-Arten auf Anophelen. [**Experiments on the Transmission of Various Types of Plasmodia by Anophelines.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1939. June. Vol. 43. No. 6. pp. 256–266.

Laboratory transmission of plasmodia by mosquitoes provides a method for the study of infective conditions. The experimental infective index so obtained is, however, of modified practical importance, since so many conditions in nature affect the course of development of the plasmodium in the mosquito. Nevertheless, facts of therapeutic interest and epidemiological significance emerge from such studies.

A. maculipennis var. *atroparvus* and var. *labranchiae* as well as *A. superpictus* were used for transmission. Exflagellation was followed under dark ground illumination and oökinetes were generally found up to 28 hours after mosquitoes had fed. For *P. vivax* transmission *A. maculipennis* var. *atroparvus* was mostly used, and sporozoites were found in the glands on the eleventh to thirteenth days. *A. superpictus* proved the best carrier for *P. falciparum*. The experiments with *P. ovale* were mostly negative and compared

unfavourably with the results of English authors. In one case of malignant tertian malaria, experiments were made after administration of $6 \times 0{\cdot}02$ gram of Certuna. Exflagellation was affected but mosquitoes could still be infected, cysts, however, were scanty. Degenerate cysts were later found in the mosquito gut. Finally the drug destroyed gametocytes.

For good mosquito infections the number of gametocytes in the blood is important and increase in the number of human passages affects these adversely. The authors consider that there is a higher mortality amongst mosquitoes heavily infected. *A. maculipennis* transmits *P. vivax* better than it does *P. falciparum*, the latter being best transmitted by *A. superpictus*. In the case of *P. vivax* transmission by *A. maculipennis* the experimental infective index was 59·3 per cent., and in that for *P. falciparum* by *A. superpictus* was 81 per cent. In the *P. ovale* experiments using *A. maculipennis* var. *labranchiae* and *A. superpictus* the results were completely negative except in one instance.

J. D. Fulton.

Robinson (G. G.). **The Mouthparts and their Function in the Female Mosquito,** *Anopheles maculipennis.—Parasitology.* 1939. July. Vol. 31. No. 2. pp. 212–242. With 9 figs. [33 refs.]

Potter (C.) & Hocking (K. S.). **An Apparatus for testing and comparing the Biological Action of Insecticides on Flying Insects and a Method for sampling the Concentration of the Atomized Insecticide.**—*Ann. Applied Biol.* 1939. May. Vol. 26. No. 2. pp. 348–364. With 8 figs.

The authors designed an apparatus in which they can subject flying insects to a very finely divided cloud of an insecticide. They appear to have had two considerations in mind: that conditions in their apparatus should be close to those which occur in practice, and that it should be possible to take a sample of the atmosphere in the apparatus at any moment.

The paper sets out in detail the construction of the chamber in which the work was done and some tests carried out with it. A cloud of insecticide in a very fine state of division is blown into this chamber. As experience shows that the concentration in the air falls rapidly at first, a short period is allowed to elapse. The experimental insects (blow-flies, mosquitoes, etc.) are then introduced into a cage which revolves inside the chamber, and keeps them in flight. At short intervals the revolving cage is brought to a standstill and a note made as to how many insects can still fly. At the end of a definite period, generally 20 minutes, the insects are removed and put on one side in order to determine how many are alive next day. After each experiment the inside of the chamber is cleaned with acetone.

The method of taking a sample from the free atmosphere inside the chamber in order to study the concentration of the insecticide is ingenious. Some coloured substance such as methylene blue is added to the insecticide. If a litre or so of air is drawn off and filtered, the whole of the dye in that sample can be recovered and estimated against tubes of known concentration. One may estimate the quantity of insecticide in a sample of air drawn off at any instant.

P. A. Buxton.

BOYD (Mark F.), KITCHEN (S. F.) & MATTHEWS (Choice B.). **Consecutive Inoculations with** *Plasmodium vivax* **and** *Plasmodium falciparum.—Amer. Jl. Trop. Med.* 1939. Mar. Vol. 19. No. 2. pp. 141–150.

Four patients inoculated with *P. vivax* were subsequently inoculated with *P. falciparum,* and four inoculated with *P. falciparum* were subsequently inoculated with *P. vivax.* In two patients of each group the subsequent inoculation was made during the incubation period of the parasite first injected ; in one of each during a clinically active attack, and in one of each following a recent attack. The results show that current or recent infection with either *P. vivax* or *P. falciparum* in no way interferes with successful infection with the other. Superinfection with the heterologous species during the incubation period gave one positive and one negative result in each group. The negative results could not be attributed to immunity of the test subjects nor are they likely to have been caused by an antagonism between the two species. The observations demonstrate the absence of cross immunity between *vivax* and *falciparum* infections. *N. W.*

SCHLESINGER (Annemarie). Ueber Beeinflussung der Blutzellgranulationen durch Milchinjektion. [**The Influence of Milk Injection on the Granulations in Blood Cells.**]—*Folia Haematologica.* 1939. Vol. 62. No. 1. pp. 137–139.

The report deals with the examination of the blood of 40 patients before and after intramuscular injection of 5–10 cc. of milk. This injection method is employed in Albania by the author, as a provocative in cases of latent malaria with negative blood examinations. Positive results are obtained in 10–15 per cent. of cases so treated.

In a number of cases studied, a few hours or longer after injection, red cells present in the circulation showed characteristic Schüffner's or Maurer's dots. In a few of these cases such stippling was definitely associated with latent *P. vivax* or *P. falciparum* infections, respectively, as verified by later finding the parasites. Most latent cases, however, as diagnosed by symptoms and history, showed only stippling in absence of parasites, following injection of milk.

Other cases with fever of unknown origin, classified as septic or toxic, showed normal erythrocytes, but had a characteristic granulation in 20–25 per cent. of mature neutrophil white cells, as a result of injection. The author considers that the parenteral administration of non-specific protein causes the granulations previously present, but not detectable, to be coarsened and rendered visible. The staining method employed was carefully controlled. *J. D. Fulton.*

LE BOURDELLÈS (B.). La sérologie du paludisme. Ses techniques actuelles. Ses applications. Ses résultats. [**Serology of Malaria: Technique, Application, and Results.**]—*Rev. Service Santé Milit.* 1939. Feb. Vol. 110. No. 2. pp. 267–297. [19 refs.]

A clearly written dissertation on malaria flocculation which takes account of most of the recently published work. It contains no new observations. *N. W.*

LENTJES (L. J. M.). Malariabehandeling met het alcaloïd hydrochinine. [**Malaria Treatment with the Alkaloid Hydroquinine.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1939. May 2. Vol. 79. No. 18. pp. 1090–1101.

Hydroquinine, a reduced quinine, with two hydrogen atoms more than quinine, has been neglected in the treatment of malaria although original reports have been uniformly favourable to its use. In the present series of 262 patients, suffering from fresh infections and not relapses, treatment consisted in a daily 3 portion dose of 0·6 gm. hydrochloride of hydroquinine, continued for exactly 7 days. The blood of all the patients was examined daily and was not pronounced negative until it was found to be free of schizonts in thick drop on 3 successive days. Freedom from fever meant that the patient's temperature did not rise above 37°C. (98·6°F.). Out of a series of 200 benign tertian cases this freedom from fever was attained after the 1st, 2nd, 3rd, 4th and 5th day by 80, 81, 35, 3, 1 patients respectively. "The influence of the drug on the schizonts was no less satisfactory." Out of 217 patients suffering from tertian malaria 41, 74, 68, 27, 6 and 1 were free of schizonts after the 1st, 2nd, 3rd, 4th, 5th and 6th days of treatment respectively. Other satisfactory features of the use of hydroquinine instead of quinine were the tolerance of the drug, the absence of such complications as deafness, tinnitus, dizziness, nausea, vomiting and diarrhoea. It would seem, therefore, according to the summary, that hydroquinine has a prompt effect on the malaria attack, an inhibiting action on the production of gametes, is capable of diminishing relapses, acts in small doses, is readily eliminated, possesses little toxicity and is generally superior to quinine. *W. F. Harvey.*

HAUER (A.). Beispiel einer familiären Form von vererbbarer Chininüberempfindlichkeit. [**Example of a Familial Form of Inherited Quinine Hypersensitivity.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1939. May. Vol. 43. No. 5. pp. 203–205. With 1 fig.

The author had under his care a female, aged 51, from Peru suffering from an old duodenal ulcer. She had an intercurrent attack of influenza, and she requested that quinine should not be administered as she was highly sensitive to it. She informed him that about half an hour after a dose of quinine severe symptoms developed, *viz.*, continuous coughing, feeling of choking and unbearable itching accompanied by urticaria involving the whole of the skin of the body. The author investigated the family history of the patient and obtained the following information. Apparently the hypersensitivity commenced in the patient's father, who lived in Peru and took small doses of quinine in the form of bark. He handed on the abnormality to the patient and her sister; the daughter of the former also suffered from hypersensitivity to quinine. The abnormality had thus been passed on through the female members of the family to the third generation. In later generations the author considers that the symptoms of hypersensitivity will increase in severity. He is of opinion that, as quinine is very largely used in the treatment of such cosmopolitan diseases as influenza, pneumonia, etc., it is important that not only should the patient inform the doctor regarding the hypersensitivity, but that there should also be a medical record to accompany the patient. *E. D. W. Greig.*

CIUCA (M.), BALLIF (L.), CHELARESCO (M.) & LAVRINENKO (N.). Contributions à l'étude du *Pl. falciparum.* (Observations sur une souche de parasite qui a subi de nombreux passages.) [**Observations on a Strain of *P. falciparum* which has undergone Numerous Passages.**]—*Arch. Roumaines Path. Expérim. et Microbiol.* Paris. 1938. Mar. Vol. 11. No. 1. pp. 85–101. With 9 graphs.

During the course of malarial therapy of general paralysis in Rumania 154 passages of a strain of *Plasmodium falciparum* were made on 1,071 patients. The majority of these were by direct blood inoculation but a number were mosquito transmissions. During all these passages no change in the morphology or virulence of the parasite was noted. In a series of tables the data relating to these infections are given—incubation periods, time of appearance of trophozoites and gametocytes, effect of treatment by quinine, atebrin or plasmoquine, the rapidity of development in mosquitoes and so on.

It is shown that in general drugs act more slowly on cases which had been infected by mosquitoes than by blood inoculations. The schizonticidal drugs, quinine and atebrin, whether combined with plasmoquine or not, did not prevent the appearance of gametocytes in a series of 149 out of 269 cases. On the other hand a single dose of plasmoquine (2 cgm.) was just as effective in getting rid of gametocytes in 53 cases as was the administration of large daily doses of this drug during the course of administration of quinine or atebrin during the attack in 110 cases. The results indicate that it is logical to administer a dose of plasmoquine (2 cgm.) three to four days after the completion of a course of schizonticidal drugs (quinine or atebrin) and to repeat this dose at five-day intervals. *C. M. Wenyon.*

BOCK (Erich). Ueber morphologische Veränderungen menschlicher Malariaparasiten durch Atebrineinwirkung. [**Morphological Changes in the Human Malaria Parasites due to Atebrin.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1939. May. Vol. 43. No. 5. pp. 209–214. With 7 figs. [11 refs.]

In a study of the changes undergone by the parasites of human malaria, including *Plasmodium ovale*, during atebrin treatment the author has noted, as others have already done, that the first is the clumping followed by extrusion of the pigment. This change may be observed, especially after intramuscular injection of the drug, within a few hours of the commencement of treatment. Further changes are the solution of the cytoplasm and the shrinking of the chromatin, which finally breaks into several separate clumps. As all the parasites react in much the same manner it would seem that the drug is one which acts directly on the parasites. *C. M. W.*

KOSTIĆ (Dušan) & ANTIĆ (Dušan). Zur Malaria-Prophylaxe mit Atebrin. [**Malaria Prophylaxis with Atebrin.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1939. July. Vol. 43. No. 7. pp. 306–311. With 1 fig.

The authors carried out prophylactic experiments with atebrin in a region of endemic malaria in Jugoslavia on 240 prisoners and warders, kept under strict surveillance. The observations were made over the whole malaria season, May till October, 86 untreated persons acted as controls, and the ages of all were between 21 and 60 years.

A. maculipennis is the chief anopheline of the region, but *A. bifurcatus* and *A. superpictus* are also found. The drug was given in 0·4 gram doses per week, half of the total being administered on two successive days. Blood examinations were made regularly. During treatment 9 cases were found infected with *P. falciparum* and 5 with *P. vivax*. At the start of the experiment the percentage showing parasites in the blood was 7·5 per cent. and at the end fell to 0·8 per cent. in treated cases. Amongst the controls the percentage of infected cases was fairly constant and rose to 46·7 per cent. in August. There were no ill-effects from the use of the drug and all treated cases were able to continue at work. *J. D. Fulton.*

SINTON (J. A.), HUTTON (E. L.) & SHUTE (P. G.). **Some Successful Trials of Proseptasine as a True Causal Prophylactic against Infection with** *Plasmodium falciparum.—Ann. Trop. Med. & Parasit.* 1939. Mar. 31. Vol. 33. No. 1. pp. 37–44. [19 refs.]

The observations described were carried out on eight patients requiring malaria therapy. Proseptasine is a benzyl derivative of sulphanilamide, para-benzylaminobenzenesulphonamide. In order to ascertain whether such malaria prophylactic properties as this drug might possess were really causal, that is operative against sporozoites and intermediate forms between sporozoites and trophozoites, the administration of the drug was in no case continued later than the day following the application of infected mosquitoes to the patient. A Rumanian strain of *P. falciparum* was employed. From 15 to 20 heavily infected *A. maculipennis* var. *atroparvus* applied to each patient assured that each received a larger dose of infection than would commonly be acquired in nature.

Three patients each received 7·5 gm. proseptasine during the 24 hours before the infecting bites and a further 4·5 gm. during the subsequent 8 hours. The discovery of a single parasite in the blood of one of these patients, on the 12th day after the bites, was the sole evidence of malaria infection in this group. An untreated control patient developed an acute attack of malaria after an incubation period of 11 days.

Two patients received 12 gm. of the drug during the 24 hours before the infecting bites and an additional 15 gm. during the subsequent 32 hours. One of these patients developed fever and parasites 22 days after the infecting bites.

Three patients received 3 gm. of the drug three times at four hourly intervals. One was bitten by infected mosquitoes immediately after the last dose, the second 24 hours later, the third 48 hours after the last dose. The first and the last of these patients developed acute attacks of malaria after incubation periods of 15 and 16 days respectively.

Thus of the 8 patients 5 showed no clinical or parasitological signs of infection though they had been under close observation from 4 to 5 months. Proseptasine appears to have a true causal prophylactic action against the strain of *P. falciparum* used. In view of the precautions necessary during treatment with sulphonamide compounds and the short duration of the prophylactic action observed, the observations have very limited practical applicability. *N. W.*

CLARK (Herbert C.). **Review of Recent Research on Drug Prophylaxis and Treatment of Malaria.**—*Southern Med. Jl.* 1939. July. Vol. 32. No. 7. pp. 685–689. [30 refs.]

MACDONALD (G.). **A Design of Flushing Siphon for Control of Anopheline Breeding.**—*Jl. Malaria Inst. of India.* 1939. Mar. Vol. 2. No. 1. pp. 63–69. With 1 text fig. & 13 figs. on 4 plates.

Inspired by the work of WILLIAMSON and SCHARFF the author has evolved a siphon for the automatic flushing of streams which has been used with success in Ceylon in the control of *A. culicifacies* breeding. Detailed scale drawings of its construction are reproduced. It is made in three parts, core, case and cover: they are each cast in concrete 2 inches thick reinforced with ⅜ inch steel rods. It is standardized and made in a central depot. It gives an automatic discharge of 475 gallons of water a minute. It can be used singly or in parallel with others. Only a low dam is required for successful operation, about 29 inches. It withstands rough treatment and is retailed at a cost of *Rs.*25 (37*s.* 6*d.*). The heaviest part of the siphon can be carried over rough country by four labourers. It is simple and ingenious and should have a wide field of application. *N. W.*

PEASTON (H.) & RENNER (E. A.). **Report on an Examination of the Spleen- and Parasite-Rates in School-Children in Freetown, Sierra Leone.**—*Ann. Trop. Med. & Parasit.* 1939. Mar. 31. Vol. 33. No. 1. pp. 49–62. With 1 map & 4 figs. on 2 plates. [10 refs.]

The results of the examination of 951 children in schools in Freetown, aged from 3 to 10 years, are recorded in this paper. The observations were made in November and December 1935, the most malarious season. The findings are compared with those of previous surveys, notably that of MACDONALD in 1926. Macdonald had found malaria to be hyperendemic in the western half of the town and endemic in the remainder. The spleen rate of the 951 children was 43 per cent., 44·1 for the endemic area and 42·6 for what had been the hyperendemic area. The corresponding parasite rates were 36·3, 34·0 and 38·5 per cent. respectively. This indicates that the hyperendemic area no longer exists and that malaria is almost equally endemic throughout the city. This improvement is ascribed to the permanent canalization of Sander's Brook and the permanent drainage of the streets draining into that water course. A brief account is given of that work.

The examination of blood films showed a remarkable predominance of *P. malariae.* Of the 345 positive blood films 167 contained *P. malariae,* 133 *P. falciparum,* 40 both *P. malariae* and *P. falciparum,* 4 *P. vivax,* and 1 *P. malariae* and *P. vivax.* *N. W.*

EATON (Monroe D.) & COGGESHALL (L. T.). **Complement Fixation in Human Malaria with an Antigen prepared from the Monkey Parasite** *Plasmodium knowlesi.*—*Jl. Experim. Med.* 1939. Mar. 1. Vol. 69. No. 3. pp. 379–398. With 4 figs. [14 refs.]

The authors have previously reported the development of specific complement fixing antibodies in monkeys infected with *P. knowlesi*

[see this *Bulletin* 1939, Vol. 36, p. 404]. In this paper observations are described on the sera of normal human beings; patients with syphilis; patients undergoing malaria therapy with either *P. knowlesi*, *P. vivax* or *P. falciparum*; and of patients suffering from naturally acquired malaria. Four *knowlesi* antigens were used prepared either from the blood or from the spleen of monkeys dying from *knowlesi* infections. The parasitized red cells were concentrated, frozen, dried and preserved in sealed tubes. The spleens were dried in a similar manner.

Antigen 1.—Dried red cells were rehydrated, 10 cc. of saline being added to the equivalent of 1 cc. of packed cells. The suspension was frozen and thawed 4 times and then centrifuged. The supernatant fluid was the antigen. It was not anticomplementary and was used in tests in a dilution 1 : 4.

Antigen 2.—Dried parasitized cells were ground in a ball mill and extracted with saline, dilution as in 1. This antigen was slightly anticomplementary and was used in tests in a dilution 1 : 10.

Antigen 3.—Prepared from dried spleen by method similar to that used in the preparation of Antigen 2, 1 gm. of dried spleen to 10 cc. of saline. It was definitely anticomplementary and was used in tests in a dilution of 1 : 10.

Antigen 4.—Dried spleen was rehydrated, 1 gm. dried spleen to 10 cc. saline, frozen and thawed as in the preparation of Antigen 1. This antigen was anticomplementary in a dilution of 1 : 2. It was used in tests in a dilution 1 : 12.

Antigen N. was prepared from normal monkey red cells with technique similar to that used in the preparation of Antigen 1.

In carrying out the tests the technique used was the same as that used for monkey sera described in a previous paper, except that 2 units of complement were used in place of 2½.

The malarial antigens gave negative complement fixation reactions with from 70 to 80 per cent. of luetic and normal sera and weak or doubtful reactions with the remainder. Some human sera gave weak positive complement fixation reactions with antigen prepared from normal monkey red cells, the percentage being slightly higher with malarial sera than with normal or luetic sera.

The most specific and sensitive antigen was Antigen 1. It gave strong complement fixation with sera of persons infected with either *P. knowlesi*, *P. vivax* or *P. falciparum*. The reaction is thus group-specific rather than species-specific.

Absorption of malarial human sera with normal monkey red cells does not remove the immune bodies which fix complement with malarial antigens. *N. W.*

MOSNA (Ezio). Contributo allo studio dell'immunità nell'infezione malarica. [**Immunity in Malarial Infection.**]—*Riv. di Parassit.* Rome. 1938. Dec. Vol. 2. No. 4. pp. 327–337. [14 refs.] English summary (10 lines).

The author has shown that the serum of monkeys suffering from chronic *Plasmodium knowlesi* infections contains immune bodies of a protective nature. If such serum is injected in large quantities into monkeys at the time of inoculation with this parasite the course of the infection is modified to the extent that it becomes chronic instead of being immediately fatal. The substances are present in the serum in small amount only. *C. M. Wenyon.*

RODHAIN (J.), with the collaboration of L. VAN HOOF & G. MUYLLE. Contribution à l'étude des plasmodium des singes africains. Les plasmodium des chimpanzés du Congo Belge. [**Plasmodia of Chimpanzees of the Belgian Congo.**]—*Ann. Soc. Belge de Méd. Trop.* 1938. June 30. Vol. 18. No. 2. pp. 237–253. With 2 charts.

The author observed in chimpanzees imported to Antwerp from the Belgian Congo malarial parasites of the types which resembled *Plasmodium falciparum* and *P. vivax*. Both these forms the author shows to be easily inoculable to uninfected chimpanzees but not to other monkeys or human beings. Previous failures to inoculate the former of these parasites to man led to the name *P. reichenowi* being given to it. Though in one case MESNIL and ROUBAUD were successful in producing a transitory infection of human *P. vivax* in a chimpanzee the failure to infect man with the chimpanzee *P. vivax*-like parasite rather suggests that it also may be a species distinct from that of man.

C. M. W.

BRUMPT (E.). Les parasites du paludisme des chimpanzés. [**The Malaria Parasites of the Chimpanzee.**]—*C. R. Soc. Biol.* 1939. Vol. 130. No. 9. pp. 837–840.

It is well known that the chimpanzee is liable to infection with malarial parasites which resemble the three well-known forms of man. This resemblance is so marked that REICHENOW and others who followed him regarded them as identical. Nevertheless the form with crescentic gametocytes was later given the name *Plasmodium reichenowi*. Recent work by RODHAIN and his co-workers has shown that while two of these chimpanzee parasites are easily inoculable to other chimpanzees, they are non-infective to man and fail to infect *Anopheles maculipennis* [this *Bulletin*, 1938, Vol. 35, p. 816.]. It would appear therefore that *P. reichenowi* and the *P. vivax*-like forms are different from the corresponding human parasites. It is probable that the *P. malariae*-like form would also be found to be uninoculable to man. Furthermore, the author of the present paper notes that there are actually certain morphological differences between the human and chimpanzee parasites. Accordingly he suggests that the *P. vivax*-like parasite of the chimpanzee be named *P. schwetzi* and the *P. malariae*-like form *P. rodhaini*, the *P. falciparum*-like parasite already having been named *P. reichenowi*. *C. M. W.*

ROUBAUD (E.), COLAS-BELCOUR (J.) & MATHIS (M.). Transmission de *Plasmodium gallinaceum* par *Aëdes geniculatus*. [**Transmission of** *P. gallinaceum* **by** *Aëdes geniculatus*.]—*Bull. Soc. Path. Exot.* 1939. Jan. 11. Vol. 32. No. 1. pp. 28–30.

It has already been shown by BRUMPT that the malarial parasite of fowls, *P. gallinaceum*, develops completely in two species of Aëdes, *viz. A. aegypti* and *A. albopictus*, both of tropical origin. The authors of the present paper show that complete development will occur also in *Aëdes geniculatus*, a tree-hole breeder of France. *C. M. W.*

HENRY (Ch.). Pouvoir infestant du sang au cours de l'incubation du paludisme de la poule (*P. gallinaceum*) inoculé par moustiques. [**Infectivity of Blood during Incubation of Fowl Malaria.**]—*Bull. Soc. Path. Exot.* 1939. Jan. 11. Vol. 32. No. 1. pp. 30–34.

After feeding mosquitoes infected with *P. gallinaceum* on two fowls, blood of these fowls was taken daily and injected into others. It was found that not till after the fourth or fifth day was the blood infective. This demonstrates that after mosquito infection there follows a latent period of four or five days before parasites are present in the blood. It is not till two days later that parasites can be detected microscopically. In discussion following the reading of this paper DECOURT states that he has noted a similar latent period following the intraperitoneal inoculation of infected blood. *C. M. W.*

HEWITT (Redginal). **Numerical Relations between Young Red Cells and Parasites throughout the Patent Period in Infections with** *Plasmodium cathemerium.*—*Amer. Jl. Hyg.* 1939. Mar. Vol. 29. No. 2. Sect. C. pp. 45–59. With 2 figs. [21 refs.]

Working with *Plasmodium cathemerium* infections in canaries, the author has been able to confirm the work of HEGNER and ESKRIDGE [this *Bulletin*, 1939, Vol. 36, p. 338] showing that a definite relationship exists between the parasites of different ages and the red cells of different types. This relationship remains fairly constant during the time that parasites are present in the blood. It means that the young malarial parasites enter young red cells only and that both achieve maturity at approximately the same time. At the time of the crises, however, there appear in the blood red cells which are exceptionally young and when these are attacked by the young parasites the latter attain maturity before the red cells are mature. *C. M. W.*

GAVRILOV (W.), BOBKOFF (G.) & LAURENCIN (S.). Essai de culture en tissus de "Plasmodium gallinaceum" (Brumpt). [**Attempt at Tissue Culture of** *Plasmodium gallinaceum.*]—*Ann. Soc. Belge de Méd. Trop.* 1938. Sept. 30. Vol. 18. No. 3. pp. 429–434.

The malarial parasite of the fowl, *Plasmodium gallinaceum*, will remain alive and retain its virulence for 21 days in defibrinated blood kept at a temperature of 0°–5°C. Under the same conditions parasites in heparinized blood were alive and infective after 10 days but not after three weeks. In spleen tissue culture of adult or embryo fowls the parasites did not survive, though they did so for 10 days in cultures of the marrow. It was determined by inoculation of infected blood into the allantoic vessels of the chick embryo at the eighth day of development that the embryo of this age is not susceptible to infection.

C. M. W.

HEGNER (Robert) & WOLFSON (Fruma). **Tissue-Culture Studies of Parasites in Reticulo-Endothelial Cells in Birds infected with Plasmodium.**—*Amer. Jl. Hyg.* 1939. Mar. Vol. 29. No. 2. Sect. C. pp. 83–87.

With a view of separating, if possible, the red cell inhabiting forms of *Plasmodium cathemerium* from the exoerythrocytic schizonts,

tissue cultures of the brain, lungs and spleen of infected birds were made. After eight days of culture the tissues were inoculated to healthy birds. These became infected with malarial parasites and showed also exoerythrocytic schizonts. It is held that the experiments were inconclusive, as even fifteen days after the cultures were made exoerythrocytic schizonts could still be detected in the macrophages, though after this interval the cultures did not produce infections.

C. M. W.

GIOVANNOLA (Arnaldo). Il *Plasmodium gallinaceum* Brumpt, i corpi toxoplasma-simili ed alcune inclusioni di probabile natura parassitaria nei globuli bianchi del *Gallus gallus*. [*P. gallinaceum*, **Toxoplasma-like Bodies and Certain Leucocytic Inclusions in Fowls.**]—*Rendiconti Istituto di Sanità Pubblica*. Rome. 1938. Vol. 1. Pt. 2. pp. 518–531. With 2 graphs & 3 plates (1 coloured). [34 refs.]

Studying *Plasmodium gallinaceum* in fowls the author has found that the cycle of development occupies 36 hours. He has also come to the conclusion that the "toxoplasma-like bodies" or the "exoerythrocytic schizonts" are actually stages in the development of the malarial parasite and not developmental stages of an independent toxoplasma. Attention is called to two kinds of inclusions probably parasitic in nature which may occur within mononuclear cells in the blood of fowls. The first resemble young stages of the malarial parasite and appear to possess one to four chromatin masses. They are rounded and stain faintly. The second have the form of deeply staining granules, rods, rings or commas, and in shape resemble organisms of the Grahamella or Eperythrozoon type. *C. M. W.*

CHORTIS (Panaiotis). Su alcuni studi di sviluppo del *Plasmodium gallinaceum* Brumpt. Nota I. [**Development of** *P. gallinaceum*.]—*Rendiconti Istituto di Sanità Pubblica*. Rome. 1938. Vol. 1. Pt. 2. pp. 532–539.

A study of the development of *Plasmodium gallinaceum* in fowls has led the author to the conclusion that the exoerythrocytic schizonts play no real part in the cycle of the parasite but are accidental and due to the phagocytic properties of the reticulo-endothelial cells, which engulf but do not destroy the young parasites. These develop abnormally and become the exoerythrocytic schizonts. *C. M. W.*

CHORTIS (Panaiotis). Sulle alterazioni del sistema reticolo endoteliale nelle infezioni da *Plasmodium gallinaceum*. [**Alterations in the Reticulo-Endothelial System in** *P. gallinaceum* **Infections.**]—*Riv. di Parassit.* Rome. 1938. Dec. Vol. 2. No. 4. pp. 315–322. With 4 text figs. & 3 coloured figs. on 1 plate. English summary (6 lines).

In malaria in fowls due to *P. gallinaceum* acute infections are characterized by a marked proliferation of the reticulo-endothelial system. Such infections may lead to profound fatal anaemia due to destruction of red cells or may become chronic with a lower degree of anaemia. If the acute infection is treated early with quinine the reticulo-endothelial response is less marked, while an anaemia of the

aplastic type is present. Exoerythrocytic schizonts are not to be regarded as normal developmental stages of the parasite. They indicate actually a loss of function of the reticulo-endothelial cells which fail to destroy completely phagocyted parasites. *C. M. W.*

RAFFAELE (G.). La fase primaria dell'evoluzione monogonica dei parassiti malarici. [**Primary Phase of the Monogony Cycle of Malarial Parasites.**]—*Riv. di Malariologia.* Sez. I. 1938. Vol. 17. No. 5. pp. 331–343. With 1 fig. [11 refs.] English summary.

Discussing the exoerythrocytic stages of bird malarial parasites the author concludes that these forms are developed either directly from sporozoites or indirectly through the products of division of these forms again infecting cells other than red cells. When the exoerythrocytic schizonts are found in birds which have been inoculated with infected blood it is not the erythrocytic forms which have produced them but the products of a previous exoerythrocytic schizogony which are present in the inoculated blood. This supposes that an exoerythrocytic schizont may give rise to two kinds of merozoites, the one (histotropic merozoites) for continuance of the exoerythrocytic development, the other (haemotropic merozoite) for the initiation of the erythrocytic development. It is further supposed that the number of haemotropic merozoites produced by exoerythrocytic schizogony increases with each such schizogony but that at any time the number of exoerythrocytic schizonts to be found is dependent on the number of histotropic merozoites produced at a previous schizogony. In favour of the occurrence of a similar cycle in human malaria the author mentions certain suggestive findings of his own in bone marrow of cases infected by sporozoite inoculation. The fact that atebrin fails to destroy the non-pigmented forms while it is active against the red cell forms in birds may have its counterpart in the failure of the drug to act as a prophylactic in human malaria. *C. M. W.*

UNGO-MUGDAN (Armida). La reazione nucleare di Feulgen negli stadi exo-eritrocitici del *P. gallinaceum* Brumpt, (1935). [**The Feulgen Reaction in the Exoerythrocytic Stages of** *P. gallinaceum.*]—*Riv. di Parassit.* Rome. 1938. Dec. Vol. 2. No. 4. pp. 323–326. With 2 coloured figs. English summary (5 lines).

The author has attempted to stain the various stages of development of *Plasmodium gallinaceum* by Feulgen's method and has found that the exoerythrocytic schizonts alone gave a definite reaction.

C. M. W.

RODHAIN (J.). L'infection à *Plasmodium relictum* chez les pingouins. [*P. relictum* **Infection in Penguins.**]—*Ann. Parasit. Humaine et Comparée.* 1939. Mar. 1. Vol. 17. No. 2. pp. 139–157. With 2 plates. [16 refs.]

The author describes an outbreak of malaria in a number of penguins in the Antwerp Zoological Gardens. The parasite, which corresponded morphologically to known strains of *Plasmodium relictum,* was readily

inoculable to canaries and from them after a number of passages back again to a penguin. A feature of the infection in the penguins was the presence in the brain and organs of large numbers of exoerythrocytic schizonts which did not occur in the canaries. The outbreak was undoubtedly due to mosquito transmission and it might have been supposed that the exoerythrocytic schizonts occurred only after sporozoite injection were it not for their occurrence also in the penguin inoculated from the canary. Of two penguins treated with atebrin one recovered. In the one that died parasites no longer occurred in the red blood corpuscles though exoerythrocytic schizonts were present in the organs. It would seem that these forms are more resistant to the drug than the ordinary blood stages. *C. M. W.*

DÉMINA (P. A.). Contribution à l'immunologie du paludisme aviaire. [**Immunology of Bird Malaria.**]—*Med. Parasit. & Parasitic Dis.* Moscow. 1938. Vol. 7. No. 4. [In Russian pp. 559–578. With 1 chart. French summary pp. 578–579.]

Working with 8 species of birds the author has shown that as regards their susceptibility to *Plasmodium relictum* they fell into three groups, the sparrow being the least susceptible, though it was more susceptible to one strain of parasite than to others. It was possible by comparing the behaviour of the three groups to different dosages of parasites or methods of inoculation to arrive at certain results having a bearing on questions of immunity and premunition. *C. M. W.*

MOSHKOVSKI (Sh. D.) & SYRKINE (S. A.). **On Morphological Alterations in Blood Elements under the Influence of Antimalarial Chemotherapeutic Preparations and Related Compounds.**—*Med. Parasit. & Parasitic Dis.* Moscow. 1938. Vol. 7. No. 3. [In Russian pp. 386–398. With 11 figs. English summary p. 398.]

Testing a number of compounds for antimalarial properties it was found that a number of the acridine series caused the appearance in the polychromatic erythrocytes of mice and birds of certain blue-staining (Giemsa and Pappenheim) granules. These stain intensely with brilliant cresyl blue in supravital staining. It is significant that it is just those compounds which are active against bird malarial parasites which cause the appearance of these small granules up to 3 microns in diameter in the red cells. *C. M. W.*

DURAND (Paul) & VILLAIN. Dérivés sulfamidés et paludisme du pigeon. [**Sulphanilamide Derivatives and Pigeon Malaria.**]—*Arch. Inst. Pasteur de Tunis.* 1939. Mar. Vol. 28. No. 1. pp. 94–95.

The authors have treated a number of pigeons harbouring *Haemoproteus columbae* with the sulphanilamide derivatives rubiazol and septoplix. The drugs were administered intramuscularly but in the doses given failed to influence the infections. *C. M. W.*

MISCELLANEOUS.

NICOLLE (P.) & SIMONS (H.). Quels services peut on attendre, en pathologie exotique, de la mesure de la vitesse de sédimentation des hématies? [**The Erythrocyte Sedimentation Reaction in Tropical Medicine.**]—*Bull. Soc. Path. Exot.* 1939. Feb. 8. Vol. 32. No. 2. pp. 223–233. [Bibliography.]

This reaction is largely used in differential diagnosis and as a measure of prognosis in numerous diseases in Europe. The authors here set out the general findings in tropical conditions. In amoebiasis the sedimentation rate is accelerated in three-quarters of the cases, and is especially related to hepatitis. In kala azar acceleration is constant; it decreases with treatment though there may be, as is not uncommon in chemotherapy, a period of exaggeration of acceleration before the return to normal. In malaria acceleration is general though there may be retardation during an acute attack. In relapsing fever the more numerous the relapses the more rapid the sedimentation. There is acceleration in Weil's disease, which serves to differentiate it from catarrhal jaundice in which sedimentation is normal. In one case of rat-bite fever the reaction was accelerated and in yaws (as in syphilis) it is rapid in the secondary and tertiary stages. In undulant fever, as in typhoid, the acceleration at first is only slight and this may be a useful point in diagnosis at a stage when serum and skin reactions are not yet positive. Sedimentation is more rapid in the nodular than in the neural forms of leprosy, and the author refers to the reaction of Rubino [see this *Bulletin*, 1939, Vol. 36, p. 691].

In trachoma there is acceleration, especially in the second stage of the disease, and in lymphogranuloma inguinale acceleration is seen more markedly in the genito-rectal than in the glandular form. If pronounced in the latter it should lead to the suspicion of extension of the disease. In yellow fever sedimentation is delayed.

There are conflicting reports in ankylostomiasis, but in tapeworm infection sedimentation is slow. In scurvy the reaction is marked. [Since the acceleration in the sedimentation rate is seen in so many diseases, its value in diagnosis, which has been claimed, is more than doubtful.] *C. W.*

MYERS (Victor C.) & EDDY (Helen M.). **The Hemoglobin Content of Human Blood.**—*Jl. Lab. & Clin. Med.* 1939. Feb. Vol. 24. No. 5. pp. 502–511. [41 refs.]

The haemoglobin content of finger capillary blood from 111 healthy adult males and 48 healthy adult females in Cleveland was determined by three methods. Firstly Newcomer's acid haematin method was used, the apparatus being calibrated against the oxygen capacity method of van Slyke. Secondly the haemoglobin was calculated from the iron content of the blood. For these determinations the samples were digested with sulphuric acid, oxidized with hydrogen peroxide and the colour developed on adding a drop of thioglycolic acid and rendering the solution strongly alkaline with ammonium hydroxide, compared colorimetrically with that developed in a standard iron solution similarly treated; the error from non-haemoglobin iron was neglected and the iron determined was assumed to be 0·335 per cent. of the haemoglobin. The third set of determinations was made by

adding diluted laked blood to a benzidine reagent, followed by hydrogen peroxide and acetic acid, the purple colour developed being compared colorimetrically with that obtained from a standard solution of blood similarly treated [*cf.* this *Bulletin*, 1938, Vol. 35, p. 449]. Agreement between the methods was good, and the average haemoglobin values were for males 15·8 gm. and for females 13·0 gm. per 100 cc. blood.

Tables are given summarizing values obtained in some 3,000 observations by various authors and the conclusion is expressed that "normal adults in good nutrition, not residing at excessive altitudes above sea level, show essentially the same concentration of haemoglobin in the blood, without difference due to race or geographic location. The only difference is that due to sex, which has long been recognised." In advanced age the values fall slightly, whereas at birth the level is very high, being 20 to 22 gm. per 100 cc. Following birth it sinks rapidly, reaching 10 gm. between the second and third month, after which it rises to 12 gm. between the fifth and six months, where it remains during childhood. The authors' figure for males agrees with the mean of the other observers given in the tables but the value for females of 13·0 gm. per 100 cc. is definitely lower than the mean of 13·8 gm. obtained from the tables; the reason for this difference is not clear. *F. Murgatroyd.*

SCHALM (L.). Ein kleiner Apparat zur Messung des mittleren Durchmessers der roten Blutzellen. [**A Small Instrument for the Measurement of the Mean Diameter of the Red Blood Cells.**]—*Klin. Woch.* 1939. Apr. 1. Vol. 18. No. 13. pp. 470–471. With 2 figs. [10 refs.]

This small halometer, designed by the author and Dr. SCHOUTEN and marketed by ZEISS, consists of a tube about 2 cm. wide and 6 cm. long. At the eye end is a half-lens which focuses a scale occupying the corresponding half of the opposite end of the tube. Adjacent to the lens is a slot to carry the blood film so that it covers the half of the field unoccupied by the lens. When any convenient but small source of light at least 3 to 4 metres away is observed through the blood film the eye accommodates so that at the same time the scale is sharply defined through the lens. The observer then sees, in the upper half of the field, half the annular diffraction spectrum produced by the blood film. In the lower half of the field he sees the scale, which indicates half of a spectrum, corresponding in size to that of a normal blood. The half-rings in the upper and lower fields are adjusted concentrically by aligning the source of light on the centre mark of the scale, and, as the two half-fields are separated only by a line, it is possible to judge whether the spectral rings produced by the blood are equal, smaller or larger in diameter than the corresponding rings of the scale representing those of a normal blood, and therefore whether the blood film under examination represents a normal, macrocytic or microcytic blood. On the right side of the scale are a number of vertical lines in relation to which the large yellow ring of the blood spectrum may be observed; reading from right to left each division represents an increase of 0·5μ over the mean cell diameter of normal blood. The instrument is designed merely for quick and rough estimations at the bedside and more accurate apparatus is recommended for precise work. *F. Murgatroyd.*

GREVAL (S. D. S.), CHANDRA (S. N.) & WOODHEAD (L. S. F.). **On M and N in Blood Groups : the Technique of Typing, the Antifluids, Findings in 300 Indians, and Associated Considerations.**—*Indian Jl. Med. Res.* 1939. Apr. Vol. 26. No. 4. pp. 1041–1054. With 1 plate.

The technique for grouping and typing blood is described in which the suspensions of cells are mixed with the sera on a slide in a moist chamber and the results read macroscopically in 5 to 15 minutes. Type sera were obtained from rabbits injected respectively with OM and ON cells from donors previously typed by means of commercial anti-M and anti-N fluids. The anti-OM and anti-ON rabbit sera were then absorbed respectively with ON and OM cells so as to obtain residual anti-M and anti-N fluids ; some degree of non-specific absorption of anti-N substance by OM cells occurs but anti-M substance does not appear to be absorbed by ON cells. The quality of fluids obtained in different experiments varied, but fluids of good potency and specificity were used to test 300 Indians in Calcutta hospitals and the following results were obtained : M 42·7 per cent., N 10·7 per cent. and MN 46·7 per cent. A small series of Europeans was typed and a table is given showing the results together with the comparative findings of other workers elsewhere. The forensic application of typing is pointed out ; factors M and N are both dominant and the genotypes of the phenotypes M, MN and N are MM, MN and NN, so that (1) the agglutinogens M and N cannot appear in the blood of a child unless present in the blood of one or both parents, and (2) a type M parent cannot have a type N child and a type N parent cannot have a type M child. Quite unrelated to these types are the iso-haemogglutinogens A and B, so that there are three types in each blood group thus making possible 12 descriptions of blood, if only the original four groups are considered, or 18 descriptions if sub-groups A_1 and A_2 are considered. It is also suggested that typing as well as grouping may be important in transfusion work. *F. Murgatroyd.*

NAPIER (L. Everard). **The Aetiology of Tropical Macrocytic Anaemia.** —*Indian Med. Gaz.* 1939. Jan. Vol. 74. No. 1. pp. 1–9. With 6 charts. [21 refs.]

Reviewing recent work the author points out that tropical macrocytic anaemia, which may not represent a homogeneous group of diseases, differs in a number of respects from pernicious anaemia. Apart from slight numbness and tingling of the toes and feet and diminished knee jerks, neurological signs are universally absent in tropical macrocytic anaemia even of extreme severity, while sore tongue and glossitis are also less common than in pernicious anaemia. The mean erythrocyte volume is high in both diseases but in the tropical anaemia the mean cell diameter is only slightly above normal, suggesting spherocytosis ; and anisocytosis and poikilocytosis are less than in pernicious anaemia. The common slight initial reticulocytosis of pernicious anaemia is absent in uncomplicated tropical macrocytic anaemia and in the latter disease the author has not seen haemoglobinized megaloblasts in the peripheral blood and only rarely in the marrow. There is a lesser tendency to leucopenia and to shift to the right in the Arneth count in tropical macrocytic anaemia than in pernicious anaemia. In the uncomplicated tropical anaemia there is said to be no increased bilirubinaemia and achlorhydria is not constant

in this disease. Yeast extract or marmite alone will produce a haemopoietic response and cure in tropical macrocytic anaemia whereas anahaemin, so potent in pernicious anaemia, sometimes fails even in massive doses; the insoluble ammonium sulphate fraction of campolon, active in pernicious anaemia, is inactive in tropical macrocytic anaemia but the soluble fraction is active in both diseases as is campolon and other "crude" liver extracts. The author believes that in tropical macrocytic anaemia there is general hyperplasia of the red cell forming elements with excessive multiplication but delayed maturation at the megalo-erythroblastic level or in other words interference with the normal development of the red cell occurs at a later stage than in pernicious anaemia. Such red cells being relatively more normal than those of pernicious anaemia are less susceptible to destruction by a normal reticulo-endothelial system and so in the uncomplicated tropical anaemia there is no excess bilirubinaemia. Where there is excessive haemolysis in tropical macrocytic anaemia the author agrees that reticulo-endothelial hypertrophy due to antecedent chronic malaria is the probable predisposing factor.

F. Murgatroyd.

EVANS (Barbara D. F.) & WILLS (Lucy). **Red Cell Fragility in Tropical Macrocytic Anaemia.**—*Jl. Path. & Bact.* 1939. Mar. Vol. 48. No. 2. pp. 437–442. With 2 charts.

The authors give the following summary :—

"(1) The uncorrected median corpuscular fragility in 40 cases of tropical macrocytic anaemia lay between 0·255 and 0·375 per cent. NaCl, with a mean of 0·316 per cent. The normal mean of 0·366 per cent., determined by the same method, is significantly higher.

"(2) The difference could be largely eliminated by applying a correction for anaemia: the range in 39 of the above cases then becomes from 0·302 to 0·428 per cent. NaCl, mean 0·356 per cent. The normal mean is only probably significantly higher than this corrected figure. The exclusion of all pregnant or recently delivered patients from the anaemia series made the difference between the mean M.C.F. of this series and that of the normal 0·0174 per cent. NaCl, standard error 0·0068, a significant difference.

"(3) The M.C.F. for mean and non-pregnant women was significantly lower than the M.C.F. of pregnant women but the number of pregnant women tested was small.

"(4) It is suggested that pregnancy may result in an increased fragility, masking the decrease which takes place in uncomplicated tropical macrocytic anaemia.

"(5) Using the corrected figures for M.C.F. there was no correlation between the degree of anaemia and the value of this figure."

DIGGS (L. W.) & BIBB (Juanita). **The Erythrocyte in Sickle Cell Anemia. Morphology, Size, Hemoglobin Content, Fragility and Sedimentation Rate.**—*Jl. Amer. Med. Assoc.* 1939. Feb. 25. Vol. 112. No. 8. pp. 695–700. With 8 figs. [16 refs.]

In sealed fresh preparations most of the cells are round or oval, although there may be a variable number of irregular, elongated or pointed cells, but as the preparation stands and carbon dioxide increases cells expand and undergo transformation to bizarre multipointed forms. This may begin within an hour and is usually completed within twelve or twenty-four hours, the rate being increased if the blood is anoxaemic. The commonest change is a rapid thickening

of the cell on one side with thinning of the disc on the opposite side; the cell diameter becomes increased and the thinned out portion pointed, while coincidently the thickened portion becomes elongated and pointed filaments extrude from its ends and side; condensation of the haemoglobin, sometimes into several foci, may occur. These preliminary changes occur within a few minutes and subsequent changes are slow. In other cells active kneading movements precede the formation of spicules, while in others no visible movement occurs until the development of barbs of cytoplasm. If the preparation is exposed to air bizarre cells revert to round form; if left sealed for some days all the cells become haemolysed or rounded up and finally disintegrated. The more mature cells sickle more readily than the less mature.

The most characteristic sickle cell is hyperchromatic, elongated, pointed at each end and curved in the middle, and may be 50μ long and only 1 to 2μ broad, the average size being from 10 to 20μ long and from 2 to 4μ broad. The number of typically sickled forms is highly variable in different patients and is not related to the severity of the anaemia. The size of the round erythrocytes in sickle cell anaemia is also highly variable, ranging from as small as platelets to as large as neutrophils, the average diameter being greater than normal. Reticulocytosis is common, the average of forty-two cases being 15 per cent. Fixed tissue preparations show sickled cells, especially in the spleen and bone marrow, and the distension of small capillaries by these cells may be a factor in the production of thrombosis, which is a common feature of this disease. The average mean corpuscular volume of forty-four cases was 90cμ, the average mean corpuscular haemoglobin 29$\gamma\gamma$ and the average mean corpuscular haemoglobin concentration 32 per cent., from which it was concluded that the erythrocytes in sickle cell anaemia are usually of the normocytic, normochromic type, with a tendency toward macrocytosis. The erythrocytes are more resistant than are normal cells to hypotonic saline but less resistant to carbon dioxide and mechanical trauma. The sedimentation rate was variable.

Dr. E. E. Osgood raised the question of differentiating true sickle cell anaemia from other anaemias in a negro with the sickle cell trait. He also stated that ovalocytosis or familial poikilocytosis occurs as commonly in white persons as in negroes, has no association, except accidentally, with anaemia and can be distinguished from true sickle cell anaemia by the fact that the cells are really sausage shaped with rounded ends and the number of poikilocytes does not increase in an atmosphere of carbon dioxide or on standing in moist cover slip preparation. Dr. L. W. Diggs stated that in true sickle cell anaemia typical oat and crescent forms can usually be found and are rarely observed in other blood dyscrasias. There is also leucocytosis, thrombocytosis and evidence of abnormal regeneration of bone marrow. The reticulocytes are increased. The erythrocytes are more resistant to hypotonic saline. There is a history of chronic anaemia, recurrent febrile illnesses with severe pains; and important physical signs are jaundice, cardiac enlargement, hepatomegaly, and ulcers of the legs. In the early stages, the spleen is enlarged but later atrophied. Patchy osteoporotic and osteosclerotic changes occur in the long bones. Usually sickle cell anaemia is not confused with other anaemias but with some acute febrile illness. In addition to ovalocytosis where the cells do not undergo further change in moist preparations, there is a

third type of abnormality characterized by elliptical cells which in moist preparations protrude points from their ends and become oat-shaped. This resembles the sickle cell trait but should not be confused with it. *F. Murgatroyd.*

PLAUT (Alfred B. J.). **Aplastic Anaemia. A Case Report.**—*South African Med. Jl.* 1939. May 13. Vol. 13. No. 9. pp. 324–327. With 1 chart.

A case of much interest, because such are rare, but seem to be becoming less so, not only in the tropics but in temperate climates also. The subject in this instance was a European, 23 years of age, admitted to hospital for epistaxis. Soon after there were haemorrhages from nose, throat, gums, ears, melaena, and later haematemesis, bleeding of the fundi and purpuric spots on legs and abdomen. Transfusion and haemostatics were practically ineffectual and death occurred 22 days after admission to hospital.

Agranulocytosis was a feature but the absence of anginose sore throat, and of mucosal or other ulceration was against this as the basal diagnosis, as was the more marked degree of anaemia. The colour index in the early stage was above unity but fell gradually to 0·87. One particularly notable feature was the rapid reduction in platelets. A week after the patient's admission to hospital they numbered 213,000 per cmm., but in less than a fortnight later were too few to estimate.

This case is referred to here because of the resemblances to onyalai [see this *Bulletin*, 1938, Vol. 35, pp. 74, 444 and 1939, Vol. 36, pp. 157–160], though the characteristic " blood blisters " in the mouth were not seen. Treatment by intramuscular injection of whole blood has had excellent results in onyalai, but was not tried in this case.

H. H. S.

MÖSCHL (Hermann). Seltene Formen von hyperchromen Anämien. [**Rare Forms of Hyperchromic Anaemia.**]—*Wien. Klin. Woch.* 1939. Apr. 21. Vol. 52. No. 16. pp. 373–378. With 1 fig. [13 refs.]

Several instances are here recorded in which the signs of hypochromic anaemia were a marked feature. Some were cases of pernicious anaemia, others were associated with ulcer of the stomach, with malignant disease and so forth, but one was of interest from the view of the tropical practitioner. This was a man of 57 years who had served in India and had suffered from malaria and at one time from abdominal pain due to appendicitis and appendicectomy had been performed. Symptoms typical of sprue now declared themselves, and red cells numbered 1,330,000 per cmm., Hb. 35 per cent., C.I., 1·3 ; anisocytosis, poikilocytosis, polychromasia, macrocytes and a few normoblasts were present. An unusual finding was gastric hyperacidity with the anaemia [but see this *Bulletin*, 1923, Vol. 20, p. 733 and 1924, Vol. 21, p. 43]. Improvement followed the administration of liver and vitamins B and C. *H. H. S.*

TROWELL (H. C.). **Diagnosis and Treatment of the Common Anaemias of Uganda.**—*East African Med. Jl.* 1939. Mar. Vol. 15. No. 12. pp. 402–418. [34 refs.]

Anaemia is probably so common in East Africa that few natives have a normal haemoglobin. Confusion may arise in the classification

of these anaemias because the average red cell of the East African native may be larger than that of the European and more work must be done on their normal and abnormal Price Jones curves. All observers are agreed, however, that the common anaemia is hypochromic. The most frequent cause appears to be hookworm infestation due exclusively to *N. americanus*. Hookworms produce anaemia by intestinal haemorrhage and if the anaemia is severe the occult blood test is always strongly positive even to several dilutions of the faecal suspension. The author believes that anaemia due to malaria is only common in persons with poor immunity, namely babies and adult immigrants; it should not be diagnosed in the absence of parasites. Malarial anaemia is haemolytic and the iron is retained in the body, whereas in hookworm anaemia there is iron loss. Many anaemias are, however, due to the operation of several different factors, hookworms, malaria and dietary deficiency, none of which can at present be quantitatively assessed. For the hypochromic anaemias 20 grains of ferrous sulphate thrice daily is satisfactory. This salt is relatively stable in solution but a few minims of sulphuric acid are added to dissolve the small amount of ferric hydroxide produced, and so preserve the appearance of the solution. [For a discussion of the cause of hookworm anaemia, see this *Bulletin*, 1937, Vol. 34, pp. 1–14.] *F. Murgatroyd.*

MACDONALD (G.). **A Study of Anaemia affecting Labourers on Assam Tea-Estates.**—*Indian Jl. Med. Res.* 1939. Apr. Vol. 26. No. 4. pp. 1001–1040. [21 refs.]

The author examined 9,042 persons on tea estates in Assam and found 10·42 per cent. of women, 5·33 per cent. of children, and 2·77 per cent. of men with an average haemoglobin of less than 50 per cent. as determined by Tallqvist's scale. He regards anaemia as the chief cause, with the possible exception of malaria, of sickness and death among the labourers and estimates that 3,000 working days and 6 lives per 1,000 persons *per annum* are lost because of it.

Contrary to common belief hookworm infection, although it may aggravate the severity or make cure more difficult, does not appear to be the chief cause of the anaemia because the degree of infestation showed a lack of correlation with the severity of the anaemia and because the effects of antihelminthic treatment on the anaemia were variable [but see this *Bulletin*, 1938, Vol. 35, p. 278, and 1939, Vol. 36, p. 324]. Other possible causes were explored in an epidemiological study.

The staple diet is rice with the addition of "dhal," a pulse resembling the lentil, and small quantities of mustard seed oil; some green vegetable and some form of animal protein are obtained by most people on one or more days of the week. Fat is deficient. The calcium intake is low and the P : Ca ratio high but the addition of calcium showed no therapeutic advantage; the iron intake is above the normal standards. Carotene and vitamin A are very deficient and this explains the high incidence of phrynoderma, xerophthalmia and night blindness; other vitamins seem adequate. The rice is either home-pounded, retaining considerable quantity of pericarp and most of the germ, or it is milled, and before either of these processes it may or may not be parboiled. An experiment showed the mean haemoglobin value of women consuming one of the four possible varieties to be as follows; home-pounded parboiled, 75·93 per cent.; home-pounded

raw, 71·72 per cent.; milled raw, 70·77 per cent.; milled parboiled, 61·10 per cent. The difference between the home-pounded parboiled and milled parboiled series is very highly significant; that between the home-pounded parboiled and milled raw series is also significant. It was considered, however, that the varying haemogenic properties of the rice were a subsidiary, and not the predominant, cause of the prevailing anaemia.

The labour force consists of those "settled" on the estates and of "short-term" recruits. The former live at a reasonably good economic level whereas the latter, despite good earnings, tend to live, often because burdened by debts in their own countries, on a pittance which may involve serious malnutrition; but contrary to normally accepted belief the incidence of anaemia was approximately equal in the two groups. It was found, however, that anaemia was significantly more frequent among both groups on estates where there was a high proportion of newly recruited labour and this suggested the possibility of an infective cause for the anaemia. Although the spleen rate showed no correlation with the incidence of anaemia it was considered that malaria might be an operative factor through the admixture of different strains of parasites or some upset in the balance between transmission and immunity following the mixture of new recruits and settlers having varying degrees of immunity.

Two experiments were designed to test this hypothesis. In the first 42 anaemic women were treated with atebrin and small doses of iron, and they showed a highly significant increase in their haemoglobin compared with controls receiving only iron. In the second experiment a search was made for malarial parasites in placental films, since only a small percentage showed parasites in the peripheral blood, but no significant correlation between anaemia and the presence of parasites was revealed.

Unfortunately, the work was prematurely terminated but the results are highly suggestive and, should the connexion between the anaemia and malaria be substantiated, reaffirm the importance of malaria control. In any case it seems desirable so far as possible to keep the old settled inhabitants and the new and temporary labourers segregated. *F. Murgatroyd.*

GIGLIOLI (George). **Health Conditions on Sugar Estates.**—*Health Conditions on the British Guiana Sugar Estates.* 1938. Nov. 21. Annexure 5. pp. v–xxx. With 8 diagrams & 2 plans.

To the Annual Report of the Surgeon-General, British Guiana for 1934, Dr. Giglioli contributed an admirable survey entitled *Medical Reorganisation and Work on the Sugar Estates* of Blairmont, Bath, and Providence [see this *Bulletin, Supplement,* 1936, p. 228*], in which he demonstrated that effective and economic preventive measures in the interests of public health can only be framed on the basis of data systematically collected over an adequate period of time. In the present paper Dr. Giglioli continues these excellent studies but this time his observations are extended to cover all sugar estates in British Guiana.

Following brief references to climatic and topographical conditions and the relevant vital statistical facts characterizing the estate populations under review, Dr. Giglioli proceeds to the detailed discussion of the several features of sanitary organization and administration,

prevalent diseases, causes of deaths, etc. These descriptions are deserving of the most careful consideration for on the present occasion it is possible to do no more than to refer briefly to one or two sections of the Report under review.

The 21 estate hospitals in British Guiana have bed accommodation for 1,246 patients, each hospital being in charge of a *Sick-Nurse Dispenser*. It is pointed out that while Dispensers are unusually well qualified to carry out what should be their work, *e.g.*, *dispensing*—their clinical training is negligible, yet on sugar estates and in rural districts in general, the work of the dispenser is mainly clinical. He is expected to diagnose and treat cases, decide which patients are to be admitted to hospital and which are to be seen by the Government Medical Officer, but the great majority of patients the dispenser treats himself as "Casual cases." In these circumstances Dr. Giglioli observes that the accuracy of diagnoses must be treated with the greatest reserve and is of the opinion that from the medico-statistical point of view estate hospital records are of questionable value. *Malaria*, which is the dominant health problem and directly or indirectly influences all other sanitary matters, is reviewed at length in this *Bulletin*, 1939, Vol. 36, p. 805, but it is pertinent to observe that during 1937 admissions to estate hospitals totalled 15,225, patients treated by G.M.O's numbered 3,135 only, while "casual cases" treated by Dispensers numbered 183,398. Among the cases treated were 42,311 of *malaria* and of these no less than 33,151, or about 79 per cent., were treated as "casual cases" by Dispensers.

The notes on the *prevailing diseases* are based on experience for the six years ending 1937, and are presented at some length. It is noted that over the period *malaria* claimed an average of 157 deaths per annum, and that *chronic nephritis* was also a serious cause of disability and death with an average of 102 deaths per annum. *Respiratory diseases* are prevalent, but the low incidence of *tuberculosis* is noteworthy with an average of only 16 deaths per annum. *Nutritional diseases* are common amongst East Indians, and *enteric fever* probably more widespread than available records would indicate.

Housing, *water supplies*, *sewage disposal*, etc., are other important matters discussed by Dr. Giglioli and for information on these matters the reader is referred to the Report itself. *P. Granville Edge.*

ORENSTEIN (A. J.). **Tropical Sanitation in its Application to Organised Industry in South Africa.**—*Public Health.* Johannesburg. 1937. Dec. pp. 13, 15, 17–21, 23.

BUTTLE (G. A. H.). **The Action of Sulphanilamide and its Derivatives with Special Reference to Tropical Diseases.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1939. July 28. Vol. 33. No. 2. pp. 141–159. With 5 figs. [93 refs.] Discussion pp. 160–168 [SINTON (J. A.), MANSON-BAHR (P.), SHARP (N. A. Dyce), LEWTHWAITE (R.), FAIRLEY (N. Hamilton), FELIX (A.) & BUTTLE (in reply)].

Since the introduction of prontosil by Domagk in 1935 there have been few branches of medicine in which sulphonamide drugs have not been employed. The sulphonamide compounds so far employed in the chemotherapy of bacterial infections can be classified into two groups. From sulphanilamide itself are derived (*a*) compounds containing substituents in the amino group, prontosil, rubiazol,

proseptasine, soluseptasine and prontosil soluble, (*b*) compounds containing substituents in the amide group, uliron, albucid and M. and B. 693. Sulphone derivatives unrelated to sulphanilamide are rodilone and 4 : 4′-diaminodiphenylsulphone : the latter, while more effective than sulphanilamide, is unfortunately more toxic. The sulphonamide group of drugs has been employed in a number of tropical infections. There is no evidence that helminthic diseases are directly affected, but in filariasis improvement is due to curative action on the secondary streptococcal invaders. *Plasmodium knowlesi* in monkeys is susceptible to sulphonamide drugs, but human malarial parasites are resistant except the sporozoites of *P. falciparum*. Trypanosomes are unaffected but a number of bacterial diseases appear to be favourably influenced by sulphonamides, more especially plague, meningococcal and pneumococcal infections. Clinical results obtained in the treatment of typhoid and Brucella infections are less satisfactory, while the only virus diseases which are in any way affected are small-pox, lymphogranuloma inguinale and trachoma, the corneal improvement in the last condition being more marked than that of the conjunctiva. The mode of action of the sulphonamide drugs is still uncertain. In the subsequent discussion, Dr. N. A. Dyce Sharp reported that he had cured five consecutive cases of tetanus with prontosil, proseptasine or sulphanilamide, given either by month or by intramuscular injection. Dr. Lewthwaite reported failure to influence tsutsugamushi disease in guineapigs but thought sulphonamide drugs might be of value in treating the bronchitis and bronchopneumonia, which are common complications of human infections ; Dr. Felix stated that in the treatment of typhoid fever the sulphonamides had been disappointing. No good results had been obtained from the use of the drugs in combination with antityphoid serum.

G. M. Findlay.

i. Debono (J. E.). **Treatment of** *Brucella melitensis* **Infection with Prontosil.**—*Brit. Med. Jl.* 1939. Feb. 18. pp. 326–327.
ii. British Medical Journal. 1939. Feb. 18. p. 342.—**Chemotherapy in Undulant Fever.**

i. In view of the favourable reports published on the effect of sulphonamides in undulant fever [see also this *Bulletin*, 1938, Vol. 35, p. 826, and 1939, Vol. 36, p. 157] the author attempted this treatment in 25 patients in Malta. In all cases the diagnosis was confirmed by agglutination reactions of over 1 in 100, and as *Brucella abortus* has not been found in Malta, all the infections may be regarded as due to *Br. melitensis*. In 12 blood culture was positive. Sixteen cases were of the ordinary type, 4 of the malignant and 6 of the mild intermittent type. In 18 prontosil rubrum was used, in 4 prontosil album and in 3 streptocide. The average dose was 4·5 gm. daily for 7 days but this was prolonged to 12 days in 4 instances, and stopped early on account of intolerance in 5.

In 19 cases there was no apparent effect on the temperature or on the course of the disease ; in the other 6 (apparently successful) cases, two relapsed (one died), one was a very mild case, in one a very small dose was given and two recovered in the 8th and 17th week respectively. In 5 instances blood culture was attempted on the 7th day of treatment, and in 4 of these it was positive, in the fifth the culture was contaminated.

The author is therefore definitely of the opinion that these drugs are not useful in undulant fever in Malta and in view of the usually low mortality of the disease and the definite element of danger in sulphonamide therapy, considers that its use is not justified.

ii. " The Editorial points out that *Br. abortus* may be more susceptible to chemotherapeutic attack than *Br. melitensis*, and that it would be unwise to compare too closely these findings, based so largely on treatment with prontosil rubrum, with others in which sulphanilamide was used, since it is generally accepted that the latter has superseded the former. A plea is made for a further trial with sulphanilamide, in a standardized system of dosage, used in alternate cases. *C. W.*

BYNUM (W. Turner). **Recurrences of Undulant Fever (Brucellosis) following the Administration of Sulfanilamide.**—*Jl. Amer. Med. Assoc.* 1939. Mar. 4. Vol. 112. No. 9. pp. 835–836.

Six cases are reported, two with acute, one with subacute and three with chronic brucellosis. The diagnosis was confirmed either by agglutination or skin tests. Sulphanilamide was given in adequate doses, but although improvement followed in three of the cases, later relapses occurred. Two of the patients experienced no relief of symptoms and one, seen first two weeks after finishing a heavy course of sulphanilamide for gonorrhoea, was not given a further course.

The author has not, therefore, been able to duplicate the satisfactory results reported by other workers. [See also this *Bulletin*, 1938, Vol. 35, p. 826, 1939, Vol. 36, p. 157, and DEBONO above.] *C. W.*

CONDELL (Lyle A.). **Sulfanilamide in Treatment of Brucellosis.**—*Southwestern Med.* 1939. June. Vol. 23. No. 6. pp. 173–176.

CLEMENTE (Giuseppe). Sulla vaccinoterapia delle Brucellosi con vaccino antimelitense Bruschettini. [**Treatment of Human Cases of Brucellosis with Bruschettini Vaccine.**]—*Riv. Sanitaria Siciliana.* 1938. Dec. 15. Vol. 26. No. 24. pp. 1436, 1439–42, 1445.

The author speaks of 40 cases and gives notes of seven infected with *Br. melitensis* in which other forms of treatment and other vaccines had been tried ineffectually, but in which much benefit followed the use of a vaccine obtained from Bruschetti Laboratory of Genoa. In some it was administered intramuscularly " the contents of a phial every 48 hours " [but the actual dosage is not stated], in others intravenously. In all it was well tolerated, but the febrile response was more marked following *intra venam* injection. *H. H. S.*

HOODLESS (D. W.). **Medical Education of Native Races.**— *Fiji Ann. Med. & Health Rep. for Year 1937.* pp. 30–32.

MCGUSTY (V. W. T.). **Note on the Central Medical School in Suva in Relation to the Health Problems of the Pacific.**—*Ibid.* pp. 33–35.

HOODLESS (D. W.). **Report on the Central Medical School, Suva.**—*Ibid.* pp. 36–40.

Hoodless discusses the education of Fijians in general and remarks that a healthy youth if taken early enough and given equal facilities

can be educated to the same extent as a European youth. He gives a brief account of the history of medical education in Fiji. McGusty states that from its inception to the end of 1936, 195 native medical practitioners have graduated from the Central Medical School. Emphasis is laid on the aim of the School to encourage the students to retain their native habits of living, as far as possible. The course lays stress on operative surgery, public health and preventive medicine. The formation of this school was only rendered possible by the pooling of the resources of the participating administrations.

Hoodless shows that in 1937 the average total cost per student was £74. In 1931 the course of study was extended from three to four years. Hospital duty is performed and lectures are given by members of the honorary staff. During the year 47 students and post-graduate students were in residence, and the average number of Fijian students who qualify each year is four, with an average annual loss of two. In Fiji there is one Native Medical Practitioner for every 1,600 of the native population. The first certificate was issued in 1888. [See, for fuller account, this *Bulletin*, 1936, Vol. 33, p. 826.] *C. W.*

DE LANGEN (C. D.). **Medical Training in the Indies.**—*Bull. Colonial Inst. Amsterdam.* 1938. Feb. Vol. 1. No. 2. pp. 125–134.

Medical instruction was first given to natives in the Netherlands Indies at Batavia in 1851 with a view to training them as vaccinators. The course was gradually extended as it was realized that these persons would be expected to do more than vaccinate, until now the medical school at Batavia attains full European standards and there is another school at Surabaya. The full course at Surabaya lasts 8 years and the graduates are fully qualified to practise in the Netherlands Indies, but not in Holland. It is intended to bring the standard at this school up to that of Batavia.

In addition to these fully qualified native doctors the authorities train subordinate assistants to act as nurses, orderlies, laboratory assistants and the like. Since these persons are not regarded as fully qualified it is unlikely that they will bring discredit on western medicine by undertaking and failing to perform efficiently tasks beyond their capacity, which might happen if a dual standard of qualification were permitted.

The author shows that modern hygiene has points in common with native custom but that western therapeutic measures are strange to the native mind, and urges that the traditional native methods of treatment, often based on experience handed down in families, should not too readily be dismissed by those with western education. He gives a warning against the use by students of advertisement literature in place of standard text-books. This practice is encouraged by the increasing amount of general pathology included in the pamphlets circulated free of charge to medical students by big business firms whose primary object is not the spread of accurate information.

The training of Asiatic medical men should be consciously directed in a manner that will fit them for their special task. The conditions differ in many respects from those which western medical men meet in Europe. [The same reasoning applies to the training of European medical men who intend to work among native races.] *C. W.*

MARTIAL (J. E.). L'acclimatement des blancs en pays chauds. Deux exemples : les maures du Hodt et la colonisation pénale en Guyane. [**Acclimatization of White Races in Hot Countries.**]—*Ann. de Méd. et de Pharm. Colon.* 1938. Oct.–Nov.–Dec. Vol. 36. No. 4. pp. 862–914. With 2 graphs.

The first part of this paper consists of a description of the climatic conditions of the French Sudan and Algeria. The second part commences by describing how, by the formation of a suitable microclimate immediately next to the skin by regulation of clothing, man is able to adapt himself to arctic and tropical conditions, in this respect differing from plants and animals. But the diseases indigenous to tropical countries constitute a greater danger than climatic conditions.

In Europe the seasons during which the heaviest agricultural work is necessary are spring and autumn, when temperatures are moderate, but in the Sudan the heavy work must be done after the first rains in May and June, at which time the sun is strong and humidity high. The effects of sunstroke and of light reflected from water, sand and other surfaces are briefly described. Humid heat is responsible for heat stroke. At 15°C. three-quarters of heat loss in man is by radiation from the skin, and one-seventh by evaporation of sweat. As external temperature rises the loss by radiation diminishes, and that by sweat evaporation increases. It is therefore obvious that the humidity of the surrounding air is the important factor. The author considers that intestinal disturbances may be attributable to chilling of the sweat during the night and that diarrhoea may result. The kidney and liver functions are disturbed.

Rainy seasons in the tropics usually coincide with hot seasons, and thus the most favourable conditions for the spread of the great endemic diseases, malaria, yellow fever and sleeping sickness, are created. Mosquitoes require water for breeding and the abundant vegetation which follows rain offers the necessary protection from the sun to the pupae of tsetse flies. Plague bacilli are best preserved in fleas at a vapour tension of 1–10 mm. and a temperature of 20–25°C., and plague incidence is greatest in the hot wet seasons.

The author considers that the resistance of peoples to indigenous diseases is a result of hereditary transmission of immunity. He quotes the mild types of yellow fever and typhus which occur in communities long exposed to these diseases, the malaria of premunized races and conversely the acute tuberculosis which may occur in native races to whom it is comparatively new.

For the white races in the tropics certain precautions are essential. Houses must provide a suitable micro-climate with protection from the sun and from disease vectors. Verandahs, thick walls, double roof and mosquito netting should be insisted upon. Clothing should be light and should not prevent the evaporation of sweat. Diet should be largely vegetarian, but transition from European diet should be gradual. Work in the open should not be undertaken in the hot damp season between the hours of 10 a.m. and 4 p.m. Prophylaxis against disease by avoidance of vectors and drug prophylaxis should be employed, and the vaccinations advised are discussed.

The author quotes the successful preventive measures applied by CASTELLANI in the Abyssinian war [see this *Bulletin*, 1938, Vol. 35, p. 628] and by the Americans in Panama, but these were disciplined communities. He gives a brief account of certain customs of the peoples

of French Africa and shows how white races (including Moors) fare badly in those parts originally inhabited by negroes, and *vice versa*. Negroes transported to Guiana show more resistance than whites. Man has not yet successfully overcome geographical barriers. [See also this *Bulletin*, 1939, Vol. 36, p. 428.] *C. W.*

ZIEMANN (Hans). Wie erobert man Afrika für die weisse und farbige Rasse ? [**Conquest of Africa for the White and Coloured Races.**]—31 pp. [Refs. in footnotes.] 1939. Leipzig : Verlag von Johann Ambrosius Barth.

ZIEMANN (Hans). Zum Problem der Akklimatisation der weissen Rasse in den Tropen. [**The Acclimatization of the White Races in the Tropics.**]—Reprinted from *C. R. Congrès Intérnational de Géographie, Amsterdam 1938.* Vol. 2. Section IIIc. pp. 357–364.

BERLIN (Ch.). **Purpura solaris.**—*Harefuah.* Jerusalem. 1939. Jan. Vol. 16. No. 1. [In Hebrew pp. 1–10. With 2 figs. English summary p. I.]

The author describes 25 cases of a condition in which haemorrhagic spots of varying size and form appear on the skin sharply outlined, and occurring on unprotected parts and particularly on the backs of the hands. They are not painful and disappear spontaneously in 5–10 days leaving no pigmentation. If pressure be made, with the thumb-nail for example, on the affected skin a "purpuric line" appears in 15–20 seconds, formed of approximated petechiae. The author believes that the condition is due to the sun's rays and suggests the name *purpura solaris*. [Nothing is said of the diet or mode of life of these patients ; the description is allied to that of various pellagroid conditions.] *H. H. S.*

MARSH (Frank). **Experiments in Heatstroke in Iran.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1938. Nov. 26. Vol. 32. No. 3. pp. 371–394. With 12 graphs. [11 refs.]

Continuing his work on experimental heat-stroke, Dr. Marsh tentatively formulates a number of important conclusions in the present paper.

The rabbit, exposed to extremely high external temperatures and unable to sweat, relies mainly on hyper-ventilation and salivation for loss of heat. But survival appears also to depend on the ability to establish a new equilibrium at a high body temperature. And this seems usually to come about without any increase in the internal heat production. Those animals which do not adapt themselves satisfactorily to the heat exhibit the usual rise in metabolism. An important factor conditioning the reaction of an animal seems to be acclimatization. Animals exposed to heat on a number of previous occasions lie quietly and accommodate themselves well.

A further important matter brought to the fore in this paper is the sensitivity of the brain to heat. Whilst brain tissue is undoubtedly amongst the tissues most sensitive to heat, the author considers its

power of survival to be greater than is usually thought. The determining factor is the period of exposure of the brain to the high temperature.

Thus the effects of heat may involve other bodily processes more seriously before damage to the central nervous system. Of the physiological processes probably concerned, the author discusses the ability of the circulatory system to withstand high bodily temperatures.

The work reported points once again to the necessity for immediately cooling the heat stroke patient. It stresses also the importance of acclimatization. *J. S. Weiner.*

ALAIN (M.) & DELBOVE (P.). Note sur deux cas d'infection à *B. whitmori* observés chez des jeunes enfants. [**Two Cases of Melioidosis in Children.**]—*Bull. Soc. Path. Exot.* 1939. Jan. 11. Vol. 32. No. 1. pp. 20–24.

The first of the cases here described is that of a child of 4 years, a European, presenting fever and diarrhoea with glairy blood-stained stools to the number of 30 in 24 hours. The child's condition became gradually worse, with insomnia, prostration and at times delirium. Six days after admission she complained of pain in the parotid region. A blood culture yielded a growth of *Pf. whitmori*. Death took place two days later.

The second was a boy of 2 years, also with diarrhoea; he showed signs of congenital syphilis. The blood contained *P. falciparum*. Four weeks after admission to hospital, without apparent cause, the child suffered from diarrhoea, 15 glairy blood-tinged stools daily, and the temperature rose to 39–40°C. From the stools *Ps. pyocyanea* was isolated which was pathogenic for guineapigs. Ten days after the onset of the diarrhoea the child developed a left-sided parotitis, and a blood culture yielded *Pf. whitmori*. Death occurred ten days later.

In neither case could any source of infection be discovered and the authors draw the strange conclusion that melioidosis is not a primary specific disease but secondary and "due to exhaltation or mutation of a saprophytic *pyocyaneus* into an organism with high pathogenicity, and capable of setting up all sorts of morbid conditions." *H. H. S.*

BAJOLET. Glossites epidémiques des pays chauds. [**Epidemic Glossitis in Warm Climates.**]—*Rev. Prat. Malad. des Pays Chauds.* 1938. Oct. 17th Year. Vol. 18. No. 10. pp. 441–4, 447–8, 451.

Epidemic glossitis has been reported from Senegal and Madagascar, but has been found also in Algeria, Tunis and France. The Senegal form is seasonal, from December to March in Senegal, during spring and summer in North Africa. It begins as a bright red circular erosion on the dorsum of the tongue near the tip, with a dusky margin. This spreads rapidly and confluence produces an appearance resembling geographical tongue. In acute cases the tongue resembles that of scarlet fever. The lesion is painless except in the acute cases, when the inside of the cheeks may be affected. Fever is uncommon.

Parotitis and involvement of the lymphatic glands may ensue, the latter persisting after the healing of the tongue. The lesions progress until the 6th or 7th day, after which they retrogress, and cure is complete in 10 to 15 days.

The Madagascar form resembles this and streptococci are always found ; it is probable that the Senegal form is also due to this organism. Treatment with sodium borate is advised and prevention by personal cleanliness and the search for carriers is advocated. *C. W.*

DEJOU (L.). Aspects cliniques de la lymphangite endémique des pays chauds. [**Clinical Aspects of Endemic Lymphangitis in Hot Climates.**]—*Rev. Prat. Malad. des Pays Chauds.* 1938. Sept. 17th Year. Vol. 18. No. 9. pp. 393–6, 399–400, 403–4, 407–8, 411.

Endemic lymphangitis, which is a streptococcal infection, must be differentiated from the lymphangitis which occurs in elephantiasis. It is an acute condition in which cellulitis accompanies the lymphangitis and may occur as nodules, which sometimes suppurate, in the subcutaneous tissues along the course of the inflamed lymphatic vessels. The corresponding glands are affected. Symptoms suggest a preliminary septicaemic phase, and this has been confirmed by the discovery of streptococci in the blood of eight of the patients. Pyaemia may occur, and may be indicated by patches of cellulitis occurring in various parts of the body. Chronic skin disease is the common precursor of endemic lymphangitis, and no doubt forms a favourable portal of entry for the streptococci.

Treatment of the skin lesions by antiseptics, especially perchloride of mercury, is the most satisfactory method of prevention. [See also *Bulletin of Hygiene,* 1939, Vol. 14, p. 508.] *C. W.*

MONTESTRUC (E.). Action de la di (P-acétylaminophényl) sulfone dans le traitement de la lymphangite tropicale. [**Di (p-Acetylaminophenyl) Sulphone in the Treatment of Tropical Lymphangitis.**]—*Bull. Soc. Path. Exot.* 1938. Oct. 12. Vol. 31. No. 8. pp. 694–695.

The success attending the use of prontosil in experimental streptococcal infections led the author and others to study several sulphur derivatives. One of these, *p*-aminophenylsulphanide (also designated 1162 F) proved even more successful than prontosil, when given in an oily suspension, to rabbits and rats with streptococcal infections and was tried in Martinique for patients with tropical lymphangitis. Still pursuing the study they evolved di (*p*-aminophenyl) sulphone (1358 F) but this, when tested in streptococcal and pneumococcal infections in mice, proved too toxic for beneficial use. They finally prepared di (*p*-acetylaminophenyl) sulphone (1399 F) to which in France is given the name Rodilone.

Brief details of three cases are given. All suffered from severe lymphangitis associated with painful erysipelatous conditions and fever. Four tablets (comprimés) of rodilone were given daily, in each case. In two of the patients the fever dropped and pain ceased in 24 hours, but treatment was continued for a week. In the other is the statement " crisis soon took place and the patient went out cured," a week after coming under treatment. The author concludes that for treatment of such cases 1399 F is a valuable addition to the physician's armamentarium. [Since it seems to be unaccompanied by any toxic

symptoms, it might be tried in cases of filarial lymphangitis. Unfortunately no indication is given as regards the dose, beyond "quatre comprimés."] *H. H. S.*

YOUNG (W. A.) & BROWN (Mary H. S.). **A Case of Esthiomène at the Sewa Hadji Hospital, Dar es Salaam.**—*East African Med. Jl.* 1938. Nov. Vol. 15. No. 8. pp. 262–266. With 3 figs. on 2 plates. [14 refs.]

A short note concerning a native woman, admitted to the hospital in Dar-es-Salaam, suffering from the genito-anal syndrome of lymphopathia venerea. No active antigen was available for cuti-reaction but the clinical picture of elephantiasis and ulceration of the pudenda with extension into the perineum and into the para-vaginal tissues can leave little doubt as to the diagnosis. No stricture of the rectum was found but breaking down buboes in the groins were present. There was a considerable degree of anaemia and a septic temperature; operative interference having proved useless, the woman died.

H. S. Stannus.

HENNESSEY (R. S. F.). **Observations on Nephritis in Uganda Natives.**—*East African Med. Jl.* 1939. Jan. Vol. 15. No. 10. pp. 329–340.

A fairly high incidence of albuminuria exists among non-nephritic hospital patients in Uganda and acute respiratory infections are responsible for a large number of these cases. Oedema may be misleading, even when associated with urine which suggests nephritis as a cause. Of 34 such cases coming to post mortem, none showed renal damage which could be held responsible for the condition, and 20 could only be ascribed to nutritional oedema.

Cardiovascular hypertrophy is often absent in the proved nephritic patients and retinal lesions are extremely rare. Blood urea is often normal but the urea concentration test is valuable. The author gives an account of the pathological findings in a series of post-mortem examinations, and shows that kidneys of normal appearance removed from non-renal cases often show proliferative glomerulitis and focal interstitial infiltrations. The common type of fatal nephritis shows proliferative hyalinizing glomerulitis, but some resemble Russell's *nephritis acris* of *repens* variety.

The progress is often insidious and the author considers that the various infections, especially pneumococcal, to which the natives of Uganda are prone, are probably aetiologically related to the local forms of nephritis. *C. W.*

LAURENT (Damien). Les problèmes de l'enfance en Afrique Equatoriale Française (années 1935–36 37). [**Child Welfare Problems in French Equatorial Africa 1935–37.**]—*Rev. Méd. et Hyg. Trop.* 1938. Mar.-Apr. & May–June. Vol. 30. Nos. 2 & 3. pp. 57–86; 121–146. With 15 figs. & 2 charts. [Summary appears also in *Bulletin of Hygiene.*]

This paper is a record of two years' child welfare work in the Middle Congo (French Equatorial Africa). It is in two parts, dealing respectively with social and medical problems.

Owing to the lack of vital statistics any estimate of infant mortality can only be approximate, but the author considers that it is at least 50 per cent. for the whole region and in places as high as 80 per cent.

Women can be induced to attend antenatal clinics with fair regularity from the fifth month onwards, but the attention they receive is largely nullified by their unwillingness to come into hospital for labour owing to the strength of tribal customs. Nevertheless, antenatal clinics are of value because through them women establish contact with the dispensaries and bring their infants during the early weeks of life when the risks are high. Early visits to the homes by health visitors do much to prevent conditions such as tetanus, ophthalmia, sepsis of the cord, and bronchopneumonia. Women are asked to bring their babies to the clinics at first twice weekly, later once a week, and the greatest importance is attached to weight as a delicate index of health.

Starvation is an important cause of infant mortality. In the early weeks the breast milk is usually quite adequate, but later, through laborious work and underfeeding, it is not. Unsuitable supplementary feeding is resorted to and the results are often disastrous. Cold, leading to respiratory affections, is a common cause of death owing to the fact that the children are naked. Dirt leads to scabies and sores and secondary infections.

The native woman is not capable of feeding her child artificially. Consequently this must be done at the centres, or in some cases prepared feeds are given to the mothers. Fortunately, the native child, even if artificially fed in a somewhat rough and ready manner, is remarkably free from digestive troubles. Clothing can be provided by voluntary effort and cleanliness inculcated by education of the mothers at the centres.

An account is given of the organization of the child welfare centres in the Brazzaville district. Records show that out of 500 infants attending the centres regularly there was a mortality in the first year of 16 per cent.

The native infant of the Congo weighs at birth less than the European, but this is made up by the end of the first month. Up to the end of the fourth month this advance is maintained, but later there is a slowing in the rate of increase and at the end of the first year the native child weighs less than the European.

Increase in height is a constant factor in the native child, and measurement is the most reliable method of ascertaining age.

Evidence of avitaminosis is found in arrested growth and oedema of the limbs. Infantile scurvy is not uncommon, and rickets is one of the great scourges. Skin affections, many of them the result of improper feeding, are very prevalent.

Prematurity is of frequent occurrence. Syphilis is not the cause and the author attributes it largely to hard manual labour in the later months of pregnancy.

Respiratory diseases are of the first importance and are the cause of nearly half the infant mortality. Clothing does much to prevent them.

Malaria is universal after the first few weeks. Splenomegaly appears early and is found in 95 per cent. of the children from two to six years, after which it diminishes. Infants respond well to quinine, which should be given only during febrile periods. The author recommends the hypodermic (not intramuscular) route for young infants.

Of the infectious diseases common in Europe, measles, whooping-cough, mumps, chickenpox, and poliomyelitis are met with ; of these

whooping-cough is the only one which is endemic and occurs throughout the year. Serious pulmonary complications of measles and whooping-cough are rare. Venereal diseases and tuberculosis, which are such a serious problem in women and children in civilized countries, are of much less importance in French Equatorial Africa.

This paper is illustrated by photographs and charts. It can be recommended to all who are interested in child welfare in Tropical Africa. *W. H. Peacock.*

REVIEWS AND NOTICES.

PORTER (Annie) [D.Sc.Lond., F.R.S.S.Af., F.L.S., etc.]. **The Larval Trematoda found in Certain South African Mollusca with Special Reference to Schistosomiasis (Bilharziasis).**—*Publications of South African Inst. Med. Res.* 1938. Dec. Vol. 8. No. 42. 492 pp. With 83 plates, 1 map & 1 fig.

With enforced interruptions, this monumental work was carried through while the writer was still on the staff of the Witwatersrand University, Johannesburg, and before she joined that of the McGill University, Montreal. Its primary aim was to determine the snails which were concerned with the spread of schistosomiasis in South Africa. But seeing that snails there contained many other cercariae than those of the schistosomes of man, that some of these others were furcocercous, and that well meaning folk, after finding fork-tailed objects in local water or in snails, had condemned the water and inflicted unnecessary hardship in a country where bathing is no mere luxury, clear descriptions of 102 cercariae found in local snails are given. Of these, 89 are listed as new species, including 16 of the 17 furcocercous forms found, and the descriptions of these cercariae occupy 274 pages ; but even so not all found are dealt with, it being felt that when material was insufficient for proper description it was better to give no name to perplex future workers trying to identify what they found.

The total number of molluscs examined, mainly in the fresh state, was nearly 7,000 belonging to 28 species, a solid foundation for conclusions. One of these last is that there is individuality even in snails and experimental animals of the same species, another way of expressing variation in nature. Thus an already infected snail rarely attracts miracidia of the same or other fluke species ; indeed in only eight of the snails examined were there larval trematodes of two species ; and individual rats vary so much in their reactions to infection that wrong conclusions may be drawn unless the habits and manners of each rat are already known. Another aspect of variability lies in the adaptation of young flukes to different snails. Thus in South Africa *S. haematobium* specially favours *Physopsis africana*, but will also use *Ph. globosa*, *Bulinus tropicus* and *Lymnaea natalensis* ; again *S. mansoni* there uses *Planorbis pfeifferi*, *Ph. africana* and *B. tropicus* ; and *S. japonicum* has been found in two specimens of *L. natalensis* collected at the same time. There is in nature a constant association of the less susceptible with the more susceptible of these snails, and this adaptability comes into action when the more susceptible species at that spot are already infected. Egg sizes are strikingly variable.

Among 1,050 eggs of *S. haematobium* measured, the lengths varied from 80μ to 185·7μ, with most between 113μ and 133μ; the widths were as variable. Next are described the egg of *S. spindale* with the larva bred in *Pl. pfeifferi*, and of *S. bovis* with the larva bred in *Ph. africana*.

On the chemical and biological side it is shown that soapy water does not kill cercariae quickly enough to prevent their finding safety in the skin, that viable eggs have been found in soil, that a relatively short storage in urine or faeces kills them, and that drainage of marshy land has stopped infection. The route of entrance of miracidia varies in South Africa. Thus *Miracidium haematobium* preferably gains entrance into the snail by the respiratory opening; but with such as penetrate the tentacle there are minute ripples lasting a few minutes which seem to mark its progress down this. *M. mansoni*, however, preferably attacks the tentacles, causing tubercles and, it may be, permanent deformity of these. The life of infected snails, as observed in the laboratory, is much shortened (presumably by that destruction of the digestive gland which is figured) and the snails are sterilized by growth of young flukes in their gonads. The copious and excellent illustrations are nearly all from drawings; and a map of the Union stippled to show the range of human infections, bears the legend that the distribution of molluscan hosts is much more extensive—a significant reminder of possibilities as ease of communication increases.

The writer points out the implications of the life-histories and leaves the application to medical men, but at the same time she tells this significant story. The children in a small Indian settlement in the Union were interested in her snail collecting, were told how the bad water made them itch, and were shown under the microscope cercariae coming out of snails; shortly the mothers came along and were told it all again, with stress thrown on the infection of the water. Next time she went that way she found that some of the pools had been filled in, others had been deepened, all the snails the people could collect had been burned, and the men had deepened the wells for drinking water.

In this monograph is summed up the investigations of thirteen years. It is a fine foundation for local work, a valuable pointer for work elsewhere in the world, and a stimulus as to what can and should be done there. For instance, is not the rarity of double infections of snails a hint of the possibility (in certain conditions and perhaps as a second line of defence) of producing in them an infection by a larval fluke which does not live in man and if possible an infection heavy enough to kill or at least to sterilize the snails? There is in this monograph much to provoke thought and aid effective action.

Clayton Lane.

GOINARD (Pierre) [Chirurgien des Hôpitaux d'Alger]. **Pathologie chirurgicale de la rate.** [Surgical Pathology of the Spleen.]—174 pp. With 4 figs. & 11 plates. 1939. Paris: Masson et Cie, 120 Boulevard Saint-Germain. [55 fr.]

This is a timely review of the present position of the surgery of the spleen, for, as the author points out, the progress of treatment of leucaemia by radiotherapy, and the modern curative treatments of pernicious anaemia and kala azar have reduced the former indications for splenectomy.

The comprehensive character of the book will appear from the fact that the injuries and diseases of the spleen are dealt with under twenty-two sections. Ptoses, torsions of the pedicle and injuries and ruptures are first dealt with, in all the more serious forms of which splenectomy is indicated. Rupture of malarial spleens is of special interest to workers in the tropics and its operative mortality is placed at about 40 per cent., which is higher than in some Indian series of cases. Under abscess of the spleen the common tropical form due to amoebiasis is only referred to and its successful treatment by aspiration and emetine is not mentioned. In the septic cases prevalent in cooler climates the mortality is placed at 80 per cent.

Some two-thirds of the book are taken up with the interesting and difficult subject of the many varieties of splenomegaly. Clinical descriptions, diagnosis, prognosis and treatment of each are given, and form a valuable contribution to the subject, as the author throughout has adopted a critical attitude regarding the resort to splenectomy for many of the forms of enlarged spleen for which it has from time to time been advised and used. In fact the only class of case for which he unreservedly claims it as a surgical triumph is haemolytic jaundice. Other splenic conditions in which it may be recommended in carefully selected cases are purpuric conditions, the forms of enlarged spleen in which splenectomy was originally advised by Banti, splenic anaemia and Gaucher's disease, and then only in the more severe types in which the prognosis under medical treatment is grave. The different varieties of cirrhosis of the liver are next dealt with. In the atrophic cirrhoses of Laennec operative procedures are ruled out. On the other hand splenectomy may sometimes be advisable in Hanot's hypertrophic cirrhosis in the presence of severe haemorrhages and anaemia, although relapses occur and the ultimate prognosis is bad. The same applies to grave forms of gastro-intestinal haemorrhages without ulceration.

The last section of the book deals with surgical procedures, by far the most frequent and important of which is splenectomy, which is simple in the case of comparatively small unadherent organs, but grave under the reverse conditions. This part of the subject is illustrated and should prove of as much service to surgeons in the tropics as other portions will be to physicians who have to advise patients regarding the possibilities of obtaining surgical relief in this difficult class of diseases. The book is well printed and in the usual paper cover of French works. *L. Rogers.*

LEWIS'S MEDICAL AND SCIENTIFIC LIBRARY. **Catalogue of Lewis's Medical & Scientific Lending Library. Part II.—Classified Index of Subjects and Authors.** New Edition. Revised to the end of 1937. —156 pp. 1939. London: H. K. Lewis & Co. Ltd., 136 Gower Street, W.C.1. [Pts. I & II complete 16*s*. (to Subscribers 8*s*.)] [Review appears also in *Bulletin of Hygiene*.]

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publication and in some cases a word or two in brackets to indicate the particular aspects of the main subjects with which the books deal. From this information a reader can readily ascertain the names of authors who have written on a particular subject, and can then, by referring to Part I of the Catalogue already published (see this *Bulletin*, 1939, Vol. 36, p. 182), obtain the full titles and some further information about the books, *i.e.* their price and size. Thus Parts I and II of the Catalogue together, besides providing subscribers with the titles of books available in Lewis's Library, form a most valuable classified guide to English published books on medical and technical subjects. *R. L. S.*

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